NATURE

No. 4216 SATURDAY, AUGUST 19, 1950 Vol. 166

CONTENTS

	Page
Control in Nationalized Industries	281
A Notable Newton Collection. By Prof. E. N. da C. Andrade, F.R.S.	284
Tunicate Biology and Development. By Dr. H. A. Cole	285
The New Vision. By Prof. W. T. Astbury, F.R.S.	285
Outline of Materialist Philosophy. By F. I. G. Rawlins	286
Wild Animals in Britain. By Miss Frances Pitt	286
Synthesis of Peptides in Enzymic Reactions involving Glutathione. By Dr. C. S. Hanes, F.R.S., F. J. R. Hird and Dr. F. A. Isherwood	288
Agricultural Genetics: Conference at Rieti	292
Obituaries:	
Dr. Fabius Gross. By Prof. James Ritchie, C.B.E.	295
Dr. J. R. Ashworth	295
Mr. Thomas Lewis. By Prof. E. A. Milne, M.B.E., F.R.S.	296
News and Views	296
Nature and Relationships of the Specific Products of the Human Blood-Group and Secretor Genes. By Dr. W. T. J. Morgan, F.R.S.	300
Sonic Disintegration of Isolated Liver Mitochondria. By George H. Hogeboom and Walter C. Schneider	302
Modification of an Anti-tubercular Molecule. By Dr. Vincent C. Barry, J. G. Belton, Rose M. Kelly and D. Twomey	303
New Simplified Electron Microscopes. By Dr. V. E. Cosslett	305
Biology and Control of Coccidiosis	306
Letters to the Editors:	
Demonstrability of the Photochemical Formation of Biradicals by Magnetic Methods.—Prof. Max Born, F.R.S., and Prof. Alexander Schönberg	307
Nickel Content of Deep-Sea Deposits.—Dr. Hans Pettersson and Henri Rotschi	308
Titrimetric Determination of Nitrates with an Equivalent Ratio of 1 : 8.—Zoltán G. Szabó and Lajos Bartha	309
Production of Staphylocoagulase in a Chemically Defined Medium.—Dr. Iwo Lominski, A. J. O'Hea, J. G. Goudie and I. A. Porter	309
A Cephalinase in Nervous Tissue.—L. W. Tyrrell	310
Effects of 'Aminopterin' on the Male Sex Organs of the Guinea Pig.—Dr. V. Traina	310
Distribution of *Chthamalus stellatus* on the Shores of North-East Ireland.—G. Williams	311
Breeding and Distribution of *Chthamalus stellatus*.—D. J. Crisp	311
The Medusa *Craspedacusta* in Australia.—I. M. Thomas	312
Birefringence of Amœbæ.—J. M. Mitchison	313
Preparation of Standardized Actinomycete Colonies.—F. A. Skinner	314
Application of the Kozeny Equation to Consolidated Porous Media.—J. E. Adamson	314
A Modification to Gabor's Proposed Diffraction Microscope.—M. E. Haine and Dr. J. Dyson	315
Geometrical Optics of Ionospheric Propagation.—Dr. K. Rawer	316
Large-scale Sporadic Movements of the E-Layer of the Ionosphere.—N. C. Gerson	316
Arc Spectrum of Gallium: New Absorption Lines in the Schumann Region.—W. R. S. Garton	317
Lead Absorption of Cosmic Rays at Different Altitudes near Magnetic Latitude 22° N.—Prof. P. S. Gill	318
Statistical Analysis of Results for Successive Tests on the same Organism.—E. J. Williams; M. J. R. Healy and F. B. Leech	319

Editorial and Publishing Offices of "NATURE"

MACMILLAN & CO., LTD.,

ST. MARTIN'S STREET, LONDON, W.C.2.

Telephone Number: Whitehall 8831

Telegrams: Phusis Lesquare London

Advertisements only should be addressed to:

T. G. Scott & Son, Ltd., Talbot House, 9 Arundel Street, London, W.C.2

Telephone Number: Temple Bar 1942

The annual subscription rate is £4 10 0, payable in advance, inland or Abroad

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CONTROL IN NATIONALIZED INDUSTRIES

THE importance of obtaining a solution of the problems of public accountability of the nationalized industries has been repeatedly emphasized in recent debates in Parliament, notably in that on Lord Lindsay of Birker's motion in the House of Lords on July 5. It is discussed at some length in the April–June issue of *The Political Quarterly*, almost the whole of which is devoted to an examination of the nationalized industries. While the criteria for the efficiency of a nationalized industry must necessarily be broad, the distinction between a solvent and an insolvent nationalized industry cannot be ignored. The taxpayer or his representative has an indisputable right to consultation before commitments (whether in wage increases or in any other way, which involve further claims on his purse, such as operating losses or increased fares) are made by an insolvent industry. In the coal industry and in the steel industry, recent emphasis has been mainly on the efficiency aspect, and, while public accountability is no less important, it is essential that it should not operate in such a way as to impair efficiency. That might well be the effect of clause 10 of the Liberties of the Subject Bill introduced into the House of Lords by Lord Samuel, which received its second reading on June 27. The clause is intended to strengthen ministerial and, in consequence, Parliamentary control over the boards of nationalized industries and services; but it would appear to permit detailed interference of a kind unlikely to do much good without at the same time making the business management of the industries more inefficient. Although Lord Samuel proposes for general adoption a practice adopted for the Port of London Authority in 1908, Lord Hall was on much stronger grounds in objecting to it on behalf of the Government than either he or the Lord Chancellor were in rejecting some of the other clauses.

The series of articles in *The Political Quarterly* represents one of the most useful contributions to public understanding of the implications of recent large-scale experiments in nationalization which have appeared since the studies on public enterprise edited by Prof. W. A. Robson, or T. H. O'Brien's "British Experiments in Public Ownership and Control" in 1937, or Dr. M. E. Dimock's "British Public Utilities and National Development" in 1933. They scarcely touch on the professional aspect, to which Prof. J. W. Cook made reference in his presidential address to the Royal Institute of Chemists on March 31; but they deal with a number of issues with which the scientific worker is closely concerned, both in his professional capacity and as a private citizen. Above all, they show how this question transcends party politics and indicate what is really at stake. If, as is pointed out in an editorial comment, "the public corporations work well and efficiently; if they display creative energy and imagination; if they show a proper concern for the divergent interests of consumers, employees and the taxpayers; if they avoid the

traditional defects of monopolies; if they excel in applying scientific research and development, then in due course an ever-increasing proportion of the nation will accept public enterprise as a wise method of conducting a larger share of the economy. But if the public corporations show themselves to be merely vast vested interests sheltered from direct parliamentary control, seated comfortably on their monopolistic positions and inflexible in outlook, the idea of public enterprise, in its present form, is likely to be rejected."

These are large questions; but answers must be found to them if the national, as distinct from sectional, interest is to be served.

The first three papers are concerned essentially with problems of organisation. Mr. D. N. Chester deals with the organisation of the nationalized industries specifically under that title; but Prof. W. A. Robson's discussion of the governing board of the public corporation and Mr. E. Davies's review of ministerial control and parliamentary responsibility of nationalized industries are no less concerned with organisation, particularly as it bears on the central problem of public accountability. Mr. Davies's article, it should be noted, was written before he became Under-Secretary of State for Foreign Affairs.

Although there is no standard form of public corporation, the main weaknesses due to organisation in the nationalized industries arise from the lack of clear division of responsibility between the Minister and the board. This, as Mr. Chester points out, is likely to cause confusion in the public mind and may lead to duplication of administrative effort. More important, it confuses the issue of public accountability, by making the evasion of responsibility easier and increasing the difficulty of securing public discussion. Even if the correct balance between interference and the autonomy of the public corporation has not yet been struck, too much appears to depend on ministerial predilection or idiosyncrasy.

Granted that each undertaking or industry must be considered on its own, and that there is no one pattern of organisation suitable for all, especially when proper attention is given to the size of the operating unit and the question of decentralization, to the vital importance of which both Mr. Chester and Mr. Davies direct attention, it should not be impossible to arrive at a clear conception of the extent and limitations of Ministerial responsibility which would permit a more rational discussion of the question of Parliamentary responsibility and control. To define more clearly the functions both of the Minister and of the board seems the first step towards devising the appropriate methods by which public accountability can be secured and both Parliament and the public be provided with the information on which to form a reasonable judgment as to the efficiency of the industry or undertaking and the extent to which the public interest is being served.

Mr. Chester suggests, indeed, that we have underestimated the importance and difficulties of the problem of size, and that much more experience is here required for sound decisions on the nature and extent of decentralization. He rightly stresses the importance of solving the problem of the right relations between the workers and the different levels of management, and the importance of developing consultative machinery at all levels. He recognizes that the boards are fully alive to these difficulties and are giving them much attention. It is probable, in his view, that the national boards may come to concentrate more and more on general policy, leaving substantially all operating responsibility to the area or local level. Mainly they may find themselves concerned with negotiations on aspects of wages and conditions which have to be settled nationally, the approval and co-ordination of the plans for capital development and re-organisation, large-scale research projects, provision of certain services, settlement of price policy, making of senior appointments, dealing with the Government, and the general supervision and co-ordination of the work of the operating units.

Mr. Chester is clearly doubtful as to the necessity of one national board owning all the assets in the industry and publicly responsible for all that is done. Some functions, he considers, could be performed by a central council; but others, such as approval of the development programme and keeping the activities of area units in line with national policy, should be the responsibility of the Minister, provided with the necessary advisory staff. A clear conception of ministerial responsibility for the exercise of public control directly over the boards, for approving the general lines of the capital development, etc., programmes, and for the collection and publication of statistics permitting public judgment of the progress and efficiency of the different boards, is the first step towards dealing with the question of public accountability with which Mr. Davies's paper is particularly concerned.

Mr. Davies points out that the considerable ministerial influence over the public corporations is exercised largely behind closed doors, and, in consequence, ministerial responsibility tends to be evaded. Mr. Davies favours more active intervention by Ministers and a greater degree of responsibility on their part to Parliament for the nationalized industries. He seems, however, to admit rather excessive use of the Parliamentary question, to an extent, indeed, that might well encroach on the administrative independence of the boards and sacrifice the advantage of having a public corporation rather than a government department. Mr. Chester's suggestion for a clearer delineation of functions and responsibilities should help to resolve this difficulty, particularly if the Ministers concerned recognize that their first responsibility is to protect the public interest and cease to regard themselves as obliged to defend the boards whenever they are attacked. Party politics, it is true, are partly to blame, and, as Mr. Davies rightly points out, the Opposition have equally misconceived the true relation between Parliament and nationalized industries, and used any failure of a particular board to attack nationalization in general. Both these papers should help to provide a more constructive and unprejudiced approach to a difficult problem, and to secure the atmosphere in which a public corporation can do its work effectively.

Prof. Robson's article is concerned particularly with the type of men and women serving on the boards of nationalized industries. A clear definition of function and responsibility is important if we are to secure the services of the right type of men or women, and while Prof. Robson holds firmly that the appointment of boards should be left to Ministers, he does not regard all the actual appointments as satisfactory. He challenges as wholly mistaken the conception of a board as the meeting-place for the representatives of interests, and suggests that Ministers have too rarely shown themselves willing or able to back their own judgment, even if it means taking a risk, rather than appoint men almost *ex officio*.

Prof. Robson recognizes the peculiar difficulties of the present situation, and that in time we may evolve a new type of directing head, differing in outlook and methods from any of those to which we are accustomed in public administration or private enterprise. Some of the new men who will direct the public corporations in the future will have been training and grown up in nationalized industries themselves. Here it will be necessary to avoid 'inbreeding', and Prof. Robson urges the encouragement of mobility between the corporations. Even with opportunities for gaining wide experience in nationalized industry, some members will be required who have worked in different fields, and Prof. Robson lays great stress on the profound and fundamental importance of upholding and enhancing the prestige, status and dignity of the posts. This consideration over-rides all those other considerations such as that of a policy rather than a functional board, and the right balance of full-time and part-time members; it is only in this way that we can hope to secure at the summit of the public corporations the men of genius and energy whose guidance is essential for the success of the industries concerned.

The composition of the national boards has likewise a most important bearing on the labour and staff problems under nationalization, which are discussed by Prof. G. D. H. Cole. Without the right men and women at the top we are unlikely to see the right personnel policy, on which, more than on any other factor, the ultimate success or failure of nationalization probably depends. Unless public corporations can evoke the public service motive throughout their vast organisations and awaken incentives of a new kind, satisfactory results from public ownership are unlikely. Prof. Cole writes with optimism on the improvement of industrial relations in the coal industry under nationalization, though he recognizes that the relations between the technical and human sides of management as well as recruitment and promotion offer some unsolved problems; and he insists that if publicly owned industries are to be conducted successfully under conditions of full employment, the co-operation of the workers and of their trade unions must be enlisted on the side of higher efficiency, and their traditional attitude of hostility to management overcome.

That, of course, bears directly on the further questions of efficiency under nationalization and its measurement, the price policy of public corporations and the voice of the consumer, to which three further articles, by Prof. P. Sargant Florence and G. Walker, Prof. W. A. Lewis and Mr. J. A. C. Griffith, are concerned. These aspects received prominence in the debate in the House of Lords on July 5, though without contributing much towards a solution. For all that was said about the responsibility of the consumers' councils, there was little constructive thought about their real relations with the boards at the national or area level, and in particular whether they are not at present doing work which would more effectively or efficiently be carried out by public relations officers, although a reference in Lord Lindsay's speech suggests that the latter point may have been in his mind.

It was clearly recognized by Lord Pakenham that the consumer councils are not fully effective; but the question was not fairly faced whether they are doing, or are even able to do, anything that could not be done in other ways. Nor was the alternative suggestion that such councils might be established on a regional basis and not on the basis of a particular industry or service, to cover the consumers' needs in the nationalized industries as a whole in a particular region, really debated. The right kind of organisation, as Lord Lindsay of Birker suggested, is one inspired by the scientific spirit; but that organisation will only be attained as the result of a scientific and impartial exploration of the whole field of possibilities.

The crucial questions of the nationalized industries are admirably brought out by Sir Arthur Salter in the concluding article. On the administrative side these are really three. Two of these have already been noted: How can the incentives of competition, with prospective profit or bankruptcy, which are found in private enterprise, be replaced, and what safeguards can be found against the inherent tendency of bureaucracy to excessive centralization? Sir Arthur does not think that they have yet received the attention they demand, although it is evident from what was said in the House of Lords debate and in the articles already noted that they are now being seriously examined.

It does not appear to be appreciated as yet, however, as Lord Lindsay pointed out, that any effective Parliamentary control demands a high degree of centralization. Much more thought will clearly have to be given to the manner of decentralization as well as to the definition of the respective functions of the boards and the Ministers if this problem of accountability and efficiency is to be solved with due regard alike to the interests of the consumer and of those employed in the nationalized industries. Here we are confronted, too, with the third problem to which Sir Arthur referred—that of the adjustment of collective bargaining to the different conditions of nationalized monopolies.

On that issue Prof. Cole had little to say; but Sir Arthur indicated the seriousness of the issues which require examination and gives just a hint of the problems for the professional man to which Prof. J. W. Cook alluded. Sir Arthur clearly regrets that some of these problems were not faced and

investigated before the latest experiments in nationalization were started, because we would then have had tentative policies, already studied and critically discussed, ready to be tried in practice.

The discussions during the past few months in various places of the activities and prospects of the nationalized industries in Britain are all to the good. They indicate, to an encouraging extent, a new disposition to re-examine the whole organisation and functioning of the industries without the strictures of party bias, and to consider in the light of actual experience how inherent dangers can be minimized or even avoided, and the arrangements for safeguarding efficiency and the public interest continuously improved.

A NOTABLE NEWTON COLLECTION

A Descriptive Catalogue of the Grace K. Babson Collection of the Works of Sir Isaac Newton and the Material relating to him in the Babson Institute Library, Babson Park, Mass.

With an Introduction by Roger Babson Webber. Pp. xiv+228+20 plates. (New York: Herbert Reichner, 1950.) 10 dollars.

IN 1710, at the age of sixty-seven, Isaac Newton moved into a house in St. Martin's Street, nearly opposite the present office of *Nature*, which he left in 1725, about two years before his death, for Kensington, in the hope that the pure air of that village, as it then was, might be better for his lungs. The St. Martin's Street house was demolished in 1913, but the dismantled fabric was saved by private action and eventually the complete woodwork of a parlour passed into the hands of Mrs. Babson, who used it to erect in the Babson Institute at Babson Park, Massachusetts, a replica of the original room. Great pains have been taken, by the installation of appropriate furniture, to give the room the appearance which it had in Newton's time. This, however, is only one expression of the Babson interest in Newton and his works. Mrs. Babson has assembled a very extensive collection of books by and about Newton, which she has supplemented by manuscripts from his hand, portraits, medals and such-like relics. The descriptive catalogue of this collection, which has just appeared, makes particulars of it accessible for the first time to students of Newton. It is an extremely handsome piece of book-making, which will be examined with interest by the cognoscenti.

This catalogue gives a literal transcription of the title-page of each book listed, a full collation, a short description of the binding and notes, in many cases taken without change from Sotheran's catalogues. The description of the binding reveals what is, in my experience, a surprisingly high proportion of original "Cambridge calf", a little-used term for calf with a rectangular panel of calf of a different colour. The transcription and collation appear to have been most carefully done—and book collectors will know how to value this. The notes, however, occasionally leave something to be desired. For example, in the short section "Collected Works", we find the three volumes of the "Opuscula", 1744, correctly listed, but described as "part of a set of 8 volumes of Newton's works collected and edited by . . . Castillioneus", with the brief titles of the "missing 5 volumes of the set". But there is no uniform eight-volume edition, with one editor, such as is suggested. The entry in Gray's "Bibliography", which has presumably misled the compilers of this catalogue, prints the title-page of the "Opuscula" with the word "Opera" erroneously substituted for the word "Opuscula". To make up the eight volumes of the "Principia", 1739–42, we have to add to the "Opuscula" not only the "Optice" of 1740, which had the same publisher but a different editor; and the "Arithmetica Universalis", which, it is true, had the same publisher and editor, but appeared in 1761, some twenty years later, in two volumes, often bound as one: but also the so-called "Jesuits' edition" of the "Principia", 1729–42, the editors of which, Le Seur and Jacquier, were not Jesuits but Minims (an order founded by St. Francis of Paula, which never had houses in England). This edition, in three volumes, sometimes bound as four, has a different publisher. It is listed as item 30 in the catalogue before us and so is not "missing". There is no evidence that the different publishers and editors issued the works with the view of making a complete edition of Newton's works: there is no uniformity of editing or publishing. It is time that the matter were made clear, and if there is, unknown to me, any "collected edition" edited by Castillioneus I hope that this declaration of opinion will bring it to light.

The notes on Voltaire's "Elémens de la Philosophie de Newton" also call for comment. They quote the phrase on the title as "Mis à la portée [porte] de tout le monde", which seems to suggest that "portée" was a misprint. It is, of course, correct—"brought within reach of everyone's comprehension". To change the word to "porte"—"shown the door by everybody"—is to perpetuate the jeer of contemporary wits. And to say of an edition of 1822, "In this last edition, wholly rewritten by Voltaire, first appeared the well-known story of the falling apple", suggests that Voltaire was still active at the great age of 128. Actually the falling apple story was printed in Voltaire's "Lettres sur les Anglais", 1733, of which the English translation, of the same year, is listed as item 242 in the volume under notice, and also in the second edition of the "Elémens de la Philosophie" of 1741, although not in the first.

The collection is a magnificent one, containing rarities, but there are many strange gaps which could be easily supplied. There is, for example, no copy of Harris's "Lexicon Technicum", in which Newton's important "De Natura Acidorum" first appeared, nor of the diary of Abraham de la Pryme, a contemporary of Newton's, in which certain well-known anecdotes of Newton were first recorded. There is a lack of books which deal with Newton's work at the Mint, such as Dana Horton's "Silver Pound". The Royal Society Tercentenary Celebrations Volume of 1946 is given, but not that of 1942. The Russian collection of papers on Newton, edited by Vavilov, is listed, but not the life of Newton by Vavilov or the Russian translation of the "Lectiones Opticæ"—the only translation of the complete work into a living tongue—which appeared at the same time. The edition of Aubrey's "Brief Lives" listed is a bad one, marred by blunders and omissions. A good edition, and all the other books mentioned—except perhaps, at the present time, the Russian ones—as well as certain other missing items, are easy to procure. Not so easy to find, perhaps, is "Eginardus" and some other of the omissions which have been

noted; but it seems a pity that so extensive a collection should have such notable gaps.

Reference must be made to the many books from Newton's library, to the noteworthy Newton manuscripts and to the many portraits in the collection, including what is apparently a fine copy of the Vanderbank portrait in the National Gallery.

The appearance of this catalogue is another sign of the informed and enthusiastic interest in Newton which is taken in the United States at the present time. The best life of Newton now available is that by L. T. More, of Cincinnati. Marjorie Nicolson's recent "Newton Demands the Muse" was an original study that gave much pleasure to students of Newton. If we have felt bound to animadvert upon certain from among the small blemishes noted in this Catalogue, nevertheless nothing set down here must be allowed to obscure the fact that this volume is a noteworthy record of a collection of great interest, which any Newton bibliophile will be glad to possess.

E. N. DA C. ANDRADE

TUNICATE BIOLOGY AND DEVELOPMENT

The Tunicata

With an Account of the British Species. By Prof. N. J. Berrill. (Ray Society Vol. for the Year 1946.) Pp. vii+354. (London: Bernard Quaritch, Ltd., 1950.) 27*s.* 6*d.*

THE appearance of Prof. N. J. Berrill's work on the tunicates is a major event for students of the group. It brings together in convenient form the results of researches by European and American workers, leavened throughout by the very substantial contributions of the author.

The book is divided into two parts, dealing respectively with the sessile and pelagic tunicates. Each part begins with a well-documented general account, followed by a synopsis of the classification with a key to the families, and, finally, by a detailed and generously illustrated account of the British species. There is a synopsis of the genera in each family, but no key to the species. This will be a disappointment to biologists unfamiliar with the group, and students must still be referred to the key given by Huus in "Die Tierwelt der Nord und Ostsee"; by a curious oversight this is not listed in the bibliography.

The treatment of the Didemnidæ is rather sketchy. The author does not refer to ten of the twelve species of *Didemnum* described in the "Faune de France", a good proportion of which, if they be confirmed as separate species, might be expected to occur in Britain; but he includes, without comment, *Didemnum gelatinosum* and gives only a very brief description of *D. maculosum*. It is by no means certain that there is such a species as *D. gelatinosum*, while *D. maculosum*, as generally recognized, includes several varieties, some of which may be accorded specific rank when more precise characters for their determination have been worked out.

In the Polyclinidæ, the author grasps the nettle more firmly and, amalgamating *Aplidium* and *Amaroucium*, discards *A. roseum* and *A. albicans* as varieties, but includes both *A. proliferum* and *A. nordmanni* and also *A. densum*. Ascidian systematists have so far failed to deal successfully with these two groups, and further progress will depend upon a careful study of the range of variability of each so-called species. In the account of the sessile ascidians, the sections on development are outstanding and are illustrated by a fine series of figures mainly from the author's publications.

The account of the pelagic tunicates is not so complete, and many of the illustrations are too small to be of real value in diagnosis. One new generic name, *Haplopleura*, is introduced for a form that is not British; a separate publication of this new name would have been advisable.

Throughout the book many of the figures reproduced from other works have been reduced and have suffered in consequence. A tendency to group too many drawings in one figure also occurs repeatedly. Errors in the text appear to be few, the worst I have noted being the sadly garbled spelling of *garstangi* in the legend to Fig. 19. The bibliography has not been so carefully checked and mis-spellings are rather numerous; there is also an error in the list of contents.

The style is eminently readable, which in itself greatly increases the value of the work; very frequently the author points to gaps in our knowledge where further research is needed. Finally, I must refer to the most remarkable feature of the book, the fact that it has been written by a busy professor of zoology at a large Canadian university; this is indeed proof of scholarship.

H. A. COLE

THE NEW VISION

Electron Microscopy

Technique and Applications. By Ralph W. G. Wyckoff. Pp. ix+248. (New York and London: Interscience Publishers, Inc., 1949.) 40*s.*

DR. WYCKOFF has achieved the sort of thing that several of us must have turned over in our minds and hoped perhaps to be able to settle down to one of these days, and we should wish to congratulate him on that in any case. He has done it exceedingly well, too, which is more to the point, and has thereby earned our thanks besides. We should have been disappointed, though, if it had turned out otherwise, for every electron microscopist knows of the industry, experience and experimental skill of R. W. G. Wyckoff.

There is, of course, a fair variety of articles and books on electron microscopy available already, and together they cover a lot of ground; but, all the same, this one is something different. The book has a relative simplicity and wide appeal which make it rather the story of the new field of vision; it contains plenty of instruction and workaday 'tips' for specialists but keeps up a fascination that many others, concerned only indirectly with particular techniques, will find irresistible. The text is authoritative but friendly, and all the time there is the background of collaboration and of the tremendous reaches still waiting to be explored. The author says, "The possible fields of application of an instrument which extends the range of our perceptions as much as does the electron microscope are so numerous, and so unpredictable, that little can be done at this early date besides indicating the kinds of objects that can be examined and the new techniques that are needed for this purpose"; but that is just what was wanted, and wanted in this kind of way, because electron microscopy is not simply a triumph of electron optics

but, in its applications, almost everybody's subject—and especially now that it has penetrated down to the molecular level, to the new underworlds of visual crystallography, visual chemistry and the like.

To-day we are recapturing with visible molecules the historic thrill that must have been experienced by Leeuwenhoek when first he perceived his "little animals". His creatures have become the monsters of our underworld, and indeed they have grown so big that we are now struggling with the problem of how best to break them down into authentic components sufficiently small for electron microscopy.

It is a pity to have to find fault in any way with this worthy effort of Dr. Wyckoff's, or rather the outcome of it; but it has to be admitted that the reproductions of his electron micrographs are scarcely as good as is required to realize to the full the inspirational value of the text. There are 202 illustrations, which means that the work is also by way of being an atlas of electron microscopy, with all the responsibility that implies. The non-specialist reader will probably judge the pictures excellent, and so they are as text-book reproductions usually go; but those who are acquainted with the great beauty and detail of some of the originals are bound to heave a sigh, and even those who are not will be puzzled sometimes to pick out what is being described. Undoubtedly it is a matter of expense, since £2 is already a substantial price for what is, after all, not a very fat book.

There is an extensive bibliography, arranged chapter by chapter. There are not many printer's errors, but a peculiar spelling aberration (also in the index) is "comma" for the optical aberration 'coma'. Occasionally, as in the legend to Fig. VIII, 1 ("Chick embryo cultured elementary bodies of a strain of psittacosis virus, etc."), there are constructions to which some of us in Britain still do not take very kindly; but that is a question of taste, or perhaps only conservatism.

W. T. Astbury

OUTLINE OF MATERIALIST PHILOSOPHY

Philosophy for the Future

The Quest of Modern Materialism. Edited by Roy Wood Sellars, V. J. McGill and Marvin Farber. Pp. xiv+657. (New York: The Macmillan Company; London: Macmillan and Co., Ltd., 1949.) 37*s.* 6*d.* net.

THE general view of the authors of this ambitious and competent work is that the power and capacity of a materialist philosophy have never been satisfactorily assessed, especially in relation to contemporary and future needs. Even without necessarily endorsing every aspect of this outlook, it is natural to extend a welcome to this book, and to see in it a solid contribution to its own particular branch of knowledge. The impression it gives—not so much in detail as in the manner of its broad sweep—is of a co-operative effort specifically designed for an American public, and one likely to win attention and hold it in the characteristic philosophical 'climate' of the United States.

With an array of some thirty contributors to consider, it is evidently unprofitable to select passages here and there for comment; better, it would seem, to attempt some assessment of the pattern as they have woven it. Thus a series of historical chapters comes first, followed by a set dealing in detail with outstanding examples of the materialist position to-day; and lastly, and perhaps the most valuable, several articles descriptive of divergent systems of thought, so divergent in fact as, for example, logical empiricism and Neo-Thomism—and all this with a common aim, kept in reasonably sharp focus.

A good feature is the way in which definite points are allowed to emerge. An illustration of this is the fervent desire of the Vienna Circle and their successors to banish metaphysics, and to make everything depend upon criteria of verifiability; as is well and truly remarked, rejection or denial of something is utterly different from 'really' getting rid of it—theories of Being are not liquidated so easily as that.

To some minds, maybe, these pages will raise more questions than they answer; it is probably well that they should. Philosophy, after all, is quite as intent upon realizing problems as in solving them.

F. I. G. Rawlins

WILD ANIMALS IN BRITAIN

Wild Animals in Britain

Mammals, Reptiles and Amphibians. By Oliver G. Pike. Pp. xii + 231 + 8 plates. (London: Macmillan and Co., Ltd., 1950.) 18*s.* net.

THE mammals of the British Isles do not make a long list; but it is a highly interesting one. On this list are found many species and subspecies that show differentiation and peculiarities due to isolation on islands. We appear to have new species in the making, this evolution proceeding under our eyes.

"Wild Animals in Britain", by Mr. O. G. Pike, another volume of the Macmillan series that deals with the British fauna and flora, covers the mammals, reptiles and amphibians and their island races.

Mr. Pike is well qualified to write on this subject, having a wide experience of British wild life, and he does so lucidly and entertainingly, giving much information that will be helpful to those interested in this branch of our fauna.

The reviewer, having a special interest in rodents, would have liked more space devoted to such small mammals as the unique Skomer vole, *Clethrionomys skomerensis*, found only on the six hundred or so acres of rocky island off the Pembrokeshire coast; but this book is a balanced survey, not an exhaustive account of any particular creature, and it admirably fulfils its purpose.

We must regret that it was not possible to include some account of certain domestic or semi-domestic animals, for example, the so-called wild white cattle, and the Chillingham herd of them in particular. These cattle are of considerable interest, being a perpetuation of a primitive type once no doubt plentiful in these islands.

But such remarks are ungrateful where so much has been given the reader, and given so charmingly.

The illustrations consist of colour plates, being reproductions of sketches, including the frontispiece from a painting by Mr. William Reeves, and a number of excellent photographs. A striking snapshot is that of a mountain hare in its form in a snowdrift by the late G. B. Kearey, and striking, too, is the photograph of a wood mouse by Dr. M. S. Wood.

Frances Pitt

Contributions to American Anthropology and History

Vol. 10, Nos. 48–51. (Publication 585.) Pp. v+186+17 plates. (Washington, D.C.: Carnegie Institution, 1949.) 4 dollars.

OF the four contributions in this volume, three deal with the Maya and the fourth with the south-west region of the United States. The first, No. 48, "The Maya Chronicles", by Alfredo Barrera Vásquez and S. G. Morley, treats of Maya history as set forth in chronicles, which have come down to us in five of the books called "Chilam Balam". These have survived in the form of seventeenth- to nineteenth-century copies of the MSS. written in Spanish characters in the Maya language, but are partly based on old hieroglyphic codexes, now lost. Mr. Barrera Vásquez has collated these sources, amending the order in some cases, and has produced an outline of the history of the Maya in northern Yucatan from the fifth to the seventeenth century. Dr. Morley adds a commentary, giving his own views of Maya history in the light of Mr. Barrera Vásquez's work. Much of this will be familiar to readers of his general work, "The Ancient Maya"; but it is valuable to have this fuller version. This contribution is of importance to all who are interested in the Maya; but the other two, by R. L. Roys, will appeal mainly to specialists.

No. 49, "Guide to the Codex Pérez", is a study of extracts made in the nineteenth century by Juan Pío Pérez from some of the books of "Chilam Balam", and No. 51, "The Prophecies for the Maya Tuns or Years in the Books of Chilam Balam of Tizimin and Mani", is a text and translation, with introduction, of the appropriate parts of those books.

Contribution No. 50, "The Pendleton Ruin", by A. V. Kidder, H. S. and C. B. Cosgrove, is an account of an excavation of a site in the extreme south-west of New Mexico belonging to a marginal variety of the Casas Grandes culture of Chihuahua, Mexico, with mention of a reconnaissance of some neighbouring sites. The work was done in 1930 and 1933, and publication has been delayed by various causes, including the death of Mr. Cosgrove. The site gave rise to the definition of the Animas Phase of the Casas Grandes culture, which is mentioned in the publications of H. S. Gladwin and others. The importance of the work lies in this and in the lack of previous work in the area.

Introduction to Chemical Thermodynamics

By Prof. Luke E. Steiner. (International Chemical Series.) Second edition. Pp. xiv+510. (New York and London: McGraw-Hill Book Co., Inc., 1948.) 36*s*.

IN this second edition of his book, Prof. L. E. Steiner has added some new material and has modified the arrangement somewhat. The section on statistical methods has been expanded into a very clear and useful chapter. The whole text is sufficiently detailed to meet the needs of all kinds of students of chemistry, and the book contains an unusual amount of information for a volume of its size.

The author has shown both originality and skill in the development of his subject. In the treatment of the First Law of Thermodynamics, energy is taken as something known, and heat and work are considered as secondary quantities in relation to it. This leads to some obscurity when the Second Law comes to be treated. The introduction to the Second Law is very clear and informative. The entropy is introduced as the coefficient of the temperature differential in the energy expression, after the manner of Gibbs; but its properties are fully developed later. This treatment, in the reviewer's opinion, leads to difficulty in relation to isothermal changes, which are particularly important in chemistry; but, apart from this, no objection can be taken to the method used by Prof. Steiner.

The applications of thermodynamics are dealt with in a very sound and detailed way, with full use of numerical data and close attention to units. There are many good numerical problems. This is a very sound and attractive book and can be recommended without reserve. J. R. P.

Alkylation of Alkanes

By Gustav Egloff and George Hulla. Vol. 1: Patents on Alkylation of Alkanes. (American Chemical Society Monograph Series, No. 107.) Pp. xiv+1138. (New York: Reinhold Publishing Corporation; London: Chapman and Hall, Ltd., 1948.) 120*s*. net.

THE chemistry of the paraffin hydrocarbons has grown enormously in recent years, chiefly owing to the study of these hydrocarbons present in petroleum. The alkylation of alkanes is of particular importance, as it is a reaction which enables one to produce branch-chain products from straight-chain hydrocarbons. This reaction thus gives a very valuable improvement in the ignition qualities of fuels for spark-ignited internal-combustion engines.

The book is the first of a three-volume treatise on the alkylation of alkanes and consists of a description and a discussion of the various patents which have been issued on this subject. Catalytic alkylation is dealt with, consideration being given to various catalysts which have been used for this purpose. There is a section dealing with the thermal alkylation of alkanes, and reactions involving the removal of alkyl radicals are also discussed.

In the two volumes to follow, it is proposed to deal with the scientific and technical publications on this subject, particularly the reports on work carried out by the oil companies during the Second World War. The complete work should be of great value as a standard reference on this subject, and will save workers in this field many hours of searching through the literature. W. W. G.

Philosophy of Nature

By Moritz Schlick. Translated by Amethe von Zeppelin. Pp. xi+136. (New York: Philosophical Library, Inc., 1949.) 3 dollars.

MORITZ SCHLICK was a leader, if not the leader, of the philosophical school known in the 1920's as the Vienna Circle. He was assassinated while on his way to lecture—an unusual death for a professor. This was in Vienna in 1936, and the assassin was a lunatic.

The book consists of an outline of a course of lectures on the concepts of natural science, compiled from MSS. left behind by Schlick. The treatment of physical concepts is clear, eminently reasonable, but elementary and much too summary. The treatment of biological concepts is perfunctory. It looks as though little of the interest of the lectures has survived in the book; a better idea of the quality of Schlick's thought can be gathered from the discussion in an appendix on "The Concept of the Atom". The publication of this book is evidently intended as an act of piety by some of Schlick's friends—a somewhat misjudged piety. A. D. RITCHIE

SYNTHESIS OF PEPTIDES IN ENZYMIC REACTIONS INVOLVING GLUTATHIONE

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FEW biological problems are of such basic interest as the elucidation of the process whereby proteins are synthesized in the cell. Despite much inquiry, however, the nature of the mechanisms involved remains obscure. Since the amino-acid residues in the protein molecule are linked together mainly by peptide bonds, the mechanism of formation of these linkages constitutes an important part of the problem as a whole.

Studies of the metabolism of 'labelled' amino-acids have shown that the proteins in living organisms are undergoing continuous breakdown and re-synthesis[1]. It is usually assumed that the down-grade process consists of hydrolysis of peptide bonds catalysed by the proteolytic enzymes; the nature of the up-grade reactions leading to the synthesis of peptides, on the other hand, has been the subject of varied speculation.

The purpose of this communication is to describe an enzymic reaction in which peptides are formed by interaction between free amino-acids and the tripeptide glutathione. The possible significance of reactions of this new type, which will be termed 'transpeptidation' reactions, can best be judged from a brief consideration of current knowledge of the subject.

Views on the Synthesis of Peptide Bonds

A hypothesis of long standing is that synthesis of peptide bonds is the result of direct condensations between carboxyl and amino-groups, in reactions which are the reversal of hydrolysis and accordingly catalysed by the proteolytic enzymes[2]. Since equilibrium between a peptide and its split products lies far on the side of hydrolysis, appreciable synthesis could occur only if the peptide were removed effectively from the system as it was formed. Bergmann and Fruton[3] recall that various proteolytic enzymes were shown to catalyse condensation as well as hydrolysis by allowing them to act upon amino-acid derivatives which yield insoluble peptides; they stress further that the sharp specificity of the proteolytic enzymes lends plausibility to the view that they may play an important part in protein synthesis, since some such specificity must be assumed to be operative during the formation of the peptide-chain structure of proteins.

According to other hypotheses, the chemical pathway of synthesis of peptide bonds is distinct from mere reversal of hydrolysis, and a variety of intermediates have been suggested, more or less tentatively, by different authors. These include: keto-aldehydes[4], acid amides[5], acyl phosphates[6], acetyl amino-acids[6], and esters of amino-acids[7].

The probable importance of mechanisms involving acyl phosphates as suggested by Lipmann[8] is evident from the discovery of three different enzyme systems in which condensations between carboxyl and amine groups take place with concomitant breakdown of adenosine triphosphate. These reactions lead to the formation of peptide-like linkages, but in no case as yet to normal peptide bonds between two alpha amino-acids; they are (*a*) the acetylation of aromatic amines by acetate and adenosine triphosphate[9], (*b*) the formation of hippuric acid from benzoic acid, glycine and adenosine triphosphate[9], and (*c*) the synthesis of glutamine, which will be discussed separately.

Glutamine and Glutathione

The enzymic synthesis of glutamine was achieved in the important studies of Speck[10a,b,c] and Elliott[11], who discovered an enzyme in animal tissues which catalyses the following reaction:

$$\text{glutamic acid} + NH_3 + ATP \rightarrow \text{glutamine} + ADP + \text{free P.}$$

Ammonia can be replaced in the reaction by hydroxylamine[10c,11], methylamine or hydrazine[10c], yielding the corresponding substituted amides. A similar enzyme is now known to occur in bacteria and in higher plants[12a,b].

Apart from the reaction leading to glutamine formation, it has been shown by isotope studies that, in the absence of adenosine triphosphate, the amide group of glutamine is exchanged with free ammonia in the presence of an enzyme from plants[13], and with hydroxylamine in the presence of enzymes from plants[12,14], animal tissues and bacteria[15]. Similar enzymic 'transfer' reactions involving asparagine have been described[16].

The close physiological connexion between glutamine (and asparagine) and the metabolism of nitrogen in both plants and animals lends great interest to these discoveries. Attention turns also to other naturally occurring γ-glutamyl compounds of which glutathione is best known. This tripeptide γ-glutamyl-cysteinyl-glycine, is widely distributed and occurs in relatively high concentration in actively growing tissues.

Various views have been advanced as to the physiological role of glutathione; but latterly emphasis has been placed upon a possible connexion with protein/amino-acid metabolism. Waelsch and Rittenberg[16], for example, suggested that glutathione may act as an intermediate between free amino-acids and proteins. Much work has been directed to the problem of the synthesis of glutathione as a model for peptide synthesis; the incorporation of 'labelled' glycine into glutathione has been used as an index of synthesis in these studies, and such incorporation has been found to occur in liver slices, homogenates and

certain cell-free extracts[17,18,19]. It has been established that the rate of incorporation of glycine is increased by addition of adenosine triphosphate[18], and quite recently, of various amides including glutamine[20]. Such studies have not as yet revealed the precise nature of the reactions involved in the synthesis of glutathione; and, it should be mentioned, the existence of transpeptidation reactions of the type to be described below may well complicate the interpretation of results based solely upon determination of rates of incorporation of 'labelled' glycine.

Possible Significance of Enzymic Transpeptidation Reactions

In planning investigations in this field, we were influenced by certain analogies drawn from the field of polysaccharide synthesis. The prominence of 'trans-glycosidation' reactions in the interconversion of various saccharides is well known, and this emphasized the desirability of determining whether corresponding enzymic reactions occur involving peptides. Such a 'transpeptidation' reaction would be pictured as a process of group transfer, without intervening hydrolysis, in which either the carboxyl- or the amino-moiety of an existing peptide would be transferred to linkage with the appropriate group of another amino-acid (or peptide) molecule. In this way a new peptide bond would be formed secondarily at the expense of an existing one according to either of the following general equations:

$$R^1.CONH.R^2 + R^3.COOH \rightleftharpoons R^3.CONH.R^2 + R^1.COOH \text{ (amine transfer)}$$

$$R^1.CONH.R^2 + NH_2.R^3 \rightleftharpoons R^1.CONH.R^3 + NH_2.R^2 \text{ (carboxyl transfer).}$$

If such enzymic transpeptidation reactions do, in fact, occur, they might clearly be of great importance in the synthesis of protein. Given a mechanism for the *primary* synthesis of a peptide bond, however limited the range of amino-acids which could thereby be linked together, it is possible to envisage a sequence of transpeptidation reactions leading to the *secondary* formation of a great variety of other peptides. It is conceivable that a regular order of occurrence of amino-acids in a chain structure could result from this process.

More detailed lines of speculation emerge when such considerations are applied to the specific findings and problems outlined earlier. It might be envisaged, for example, that relatively few mechanisms exist for the primary synthesis of peptide or peptide-like bonds, and that glutamine, and possibly in addition γ-glutamyl peptides formed in a similar way, are examples of such primary products. The secondary derivation of any particular peptide might then be pictured as involving any or all of the following transpeptidation reactions:

(*a*) γ-glutamyl-amide ⇌ γ-glutamyl-peptide (carboxyl transfer);

(*b*) γ-glutamyl-peptide 1 ⇌ γ-glutamyl-peptide 2 (carboxyl transfer);

(*c*) γ-glutamyl-peptide ⇌ α-peptide (amine transfer);

(*d*) α-peptide 1 ⇌ α-peptide 2 (amine *or* carboxyl transfer).

As an example of a type (*a*) reaction it would be possible to envisage the formation of glutathione by the transfer of the γ-glutamyl group from glutamine to cysteinyl-glycine (carboxyl transfer). The same tripeptide might be formed in other ways, for example, by the transfer of glycine from some suitable peptide to the carboxyl group of γ-glutamyl-cysteine (amine transfer).

In the course of a sequence of such reactions (whether *a* to *c*, *b* to *c*, or a sequence of type *d* reactions), the constituent groups of the first peptide would be set free. Thus re-synthesis of this peptide by a primary mechanism would permit the continuation of the process.

This speculative scheme formed the starting point of a series of investigations of which one result has been the demonstration that transpeptidation reactions of type *b* do, in fact, occur. Thus glutathione has been found to react with free amino-acids (and possibly other peptides) giving rise to other γ-glutamyl peptides.

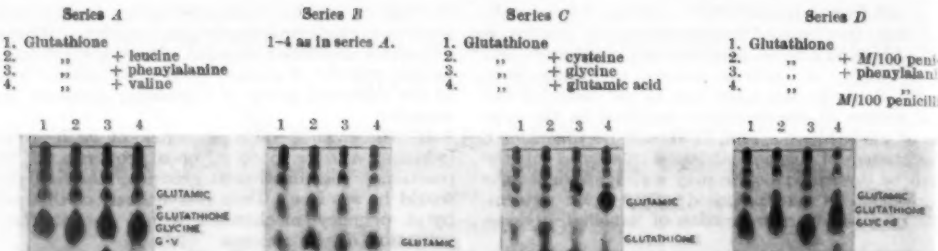
Demonstration of Transpeptidation Reactions involving Glutathione

Extracts of kidney and pancreas tissues are known to contain enzymes which act upon glutathione[21,22,23]; and the reaction has been pictured as a relatively simple process of degradation involving first the splitting of the γ-linkage to yield glutamic acid and cysteinyl-glycine, followed by hydrolysis of the latter[23]. This is undoubtedly an over-simplified picture of the complex reactions which occur in such systems.

In the present experiments, enzymes prepared from sheep kidney have been used. 6 gm. of fresh tissue are homogenized with 10 ml. *M*/20 potassium phosphate buffer at *p*H 7·4, containing *M*/1,000 magnesium ion. After centrifuging (15 min., 3,000 r.p.m.) the supernatant is dialysed against 1 litre of buffer for 4 hr. with stirring. In the typical enzymic digest, such extracts diluted to one-third original strength were allowed to act upon glutathione (*M*/20 final concentration) or glutathione (*M*/20) plus selected amino-acid (*M*/20) at 32° C.

Reaction was detected and followed by paper chromatography using Whatman No. 1 paper (either as supplied or after washing in *M* sodium carbonate followed by water) and for most purposes 80 per cent aqueous propanol as solvent. Cysteine and peptides containing cysteine presented chromatographic difficulties which were overcome by coupling with N-ethyl-maleimide[24] during the preparation of samples as follows: samples of digests (0·3 ml.) were treated with 0·6 ml. warm ethanol to precipitate proteins; the supernatant solution was evaporated in a desiccator and the residue taken up in 0·15 ml. *M*/7·5 N-ethyl-maleimide in water[24]. The resulting solution was used for spotting on the chromatogram, using 1 μl.

Chromatograms illustrating the main points to be discussed are shown in the accompanying reproduction, those in any one series (for example, *A*, *B*, etc.) being comparable as to enzyme, paper, running-time, etc. In all cases illustrated, the enzymic reaction had proceeded 60 min. when the samples were taken. Control chromatograms of enzyme without additions of substrate showed no ninhydrin-reacting material; the various substrates were pure, and when run alone or with killed enzyme they gave compact spots in characteristic positions (except that glutathione on one batch of unwashed paper tended to give a double spot on prolonged running); an



CHROMATOGRAMS OF ENZYMIC DIGEST SAMPLES

Digests consisted of: kidney enzyme, ½ vol.; substrates as indicated added in *M*/20 final concentration; phosphate buffer *p*H 7·4—*M*/60. Samples prepared for analysis as described in text after 60 min. reaction at 32° C. Chromatography: Solvent: propanol/water (80/20); papers: series *C*, No. 1 Whatman unwashed; series *A*, *B* and *D*, No. 1 washed in sodium carbonate; running times: series *A* and *C*, 19 hr.; series *B* and *C*, 43 hr.

identification mixture of glutamic acid, glutathione, glycine, cysteinyl-glycine and cysteine was run consistently on all papers, and the position of these substances is indicated beside each series. Oxidized glutathione (*G* – S – S – *G*) remains almost at the starting line on the chromatogram and could not be confused with the other substances to be discussed.

The complexity of the 'breakdown' of glutathione under the action of these extracts will be evident from chromatograms *A*1, *B*1, *C*1.

In each digest there remains only a small and somewhat variable spot of glutathione (see series *C*) and each shows a prominent glycine spot; a relatively small amount of glutamic acid has been liberated, and cysteine, ranging from a trace to a pronounced spot, is present. The striking feature of all cases, however, is the series of at least three substances which travel as compact spots more slowly than glutamic acid. Discussion of the nature of these substances is best deferred until the interaction between glutathione and added amino-acids is established. It should be mentioned that chromatograms of digest samples taken after shorter reaction periods showed more or less pronounced spots of cysteinyl-glycine, these diminishing and finally disappearing as the reaction proceeds.

In a series of four digests, the enzyme was incubated with glutathione alone, glutathione plus leucine, glutathione plus phenylalanine, and glutathione plus valine; analysis of these on carbonate-washed paper run for 19 and 43 hr., respectively, are shown in series *A* and *B*. The three amino-acids added were chosen because of their relatively rapid rates of travel, as will be seen from their positions on the chromatograms. (Leucine had run off the paper in series *B*.) In both series new spots intermediate in position between glycine and cysteine were present in digests to which amino-acids were added with glutathione; these new substances are different in the three cases, and it will be noted that they travel in the same relative order as the added amino-acids. (The new spot in *A*4 has scarcely separated from glycine; but a clear separation had occurred in *B*4.) The three new spots formed in these digests are believed to be, respectively, γ-glutamyl-leucine (*G*-*L*), γ-glutamyl-phenylalanine (*G*-*Ph*) and γ-glutamyl-valine (*G*-*V*).

The provisional identification of these substances formed by the interaction of glutathione with the different added amino-acids rests at present upon a closer study of the middle member of the series. Analysis of samples after varying periods of enzymic action show that the new substance increases progressively during the 60 min. of reaction period. Rows of spots of the new substance formed with glutathione plus phenylalanine as substrate were extracted from the paper; this extracted material was unchanged as regards its chromatographic behaviour. A portion was hydrolysed (6*N* hydrochloric acid, 105° C., 24 hr.) and the resultant solution was found to contain only glutamic acid and phenylalanine. Glutamic acid was then identified as the amino end-group by Sanger's method[25].

These various lines of evidence pointed to the new substance being either α- or γ-glutamyl-phenylalanine.

A specimen of the former dipeptide was prepared for comparison. The unknown, although similar in chromatographic behaviour in the aqueous propanol solvent, was not identical, and by using propanol/glacial acetic/water (80/10/10) as solvent a clear separation was obtained, the α-peptide travelling appreciably faster than the unknown (as would be expected on the basis of the *pKa* values of the two carboxyl groups if the unknown were the γ-peptide). A further important point of difference was that the α-peptide was broken down rapidly to glutamic acid and phenylalanine by the enzyme preparation. Pending the preparation of γ-glutamyl-phenylalanine for direct comparison, there thus seem good grounds for provisional identification of the unknown with this dipeptide.

In a further series of four digests of which the chromatograms are shown in series *C*, the enzyme was incubated with glutathione alone, and glutathione plus additions of each of its constituent amino-acids in turn. (These chromatograms were run with solutions of half the usual strength as this improved the definition.)

It will be seen that *C*4 shows not only the heavy spot of the added glutamic acid, but also a spot near the starting point which is much heavier than with glutathione alone. Similarly, *C*2, with added cysteine, shows not only a cysteine spot but also intensification of certain of the slowly moving spots. Finally, *C*3 shows that the effect of adding glycine is to increase strikingly the amount of the spot travelling immediately above glutamic acid.

These observations suggest strongly that the slowly travelling spots which appear when glutathione is incubated with the enzyme represent peptides formed by the interaction of glutathione with its different constituent amino-acids. Given any trace of amino-acids in the digest, it is probable that the transpeptidation reaction occurs, liberating cysteinyl-glycine, which is then split to cysteine and glycine. Further transfer of γ-glutamyl groups from glutathione to these amino-acids would then occur more rapidly. Since there are indications that these slowly moving substances may be more complex than dipeptides, no suggestions will be made as to their identity until quantitative analyses are available.

At the suggestion of Dr. E. F. Gale, a study of the effect of benzyl penicillin on the system has been made. Kimmel, Olson, Okeson and Binkley[26] have reported recently that the breakdown of glutathione in a similar enzymic preparation is inhibited competitively by benzyl-penicillin.

Series *D* chromatograms illustrate typical results. By comparing *D*1 with *D*2 (from digests with glutathione alone) and *D*3 with *D*4 (from digests with glutathione + phenylalanine) the following main effects of the addition of benzyl-penicillin will be seen: (1) the amount of residual glutathione is greater, thus confirming the conclusion of Kimmel *et al.* (*loc. cit.*); (2) the cysteine spot has largely disappeared, due presumably to the well-known reaction between cysteine and penicillin[27]; (3) two of the slowly moving spots characteristic of the breakdown of glutathione have virtually disappeared; (4) the formation of γ-glutamyl-phenylalanine is strongly inhibited.

These results suggest that the biological action of penicillin may be connected with the inhibition of γ-glutamyl transfer reactions; but, in addition, the combination of penicillin with cysteine would prevent the re-synthesis of glutathione from its breakdown products and so interrupt any cyclical process in which it is involved.

Mention should be made finally of experiments carried out with other types of enzyme preparation. Pig kidney, acetone powder from sheep kidney, and fresh ox pancreas were found to give active extracts. No detectable activity was found in extracts of liver.

Discussion

One of the four main types of transpeptidation reactions which have been postulated can now be said definitely to occur, and the participation of glutathione in such reactions has been demonstrated.

The exploration of other parts of the scheme of reactions relating to γ-glutamyl compounds is in progress, and it remains to be seen whether, on one hand, there is a direct biochemical connexion between glutamine and glutathione and whether, on the other hand, γ-glutamyl peptides may be converted further into α-peptides as a result of 'amine transfer' reactions.

In the meantime, attention may be directed to the striking fact that, not only is the γ-linkage itself stable against the action of peptidases present in the extracts used, but also the presence of the γ-glutamyl group in glutathione renders the cysteinyl-glycine linkage immune from attack by peptidases (cf. Binkley and Nakamura[23]). This type of effect may well be of some general importance in the intact cell, since it forms a mechanism whereby peptides may be protected from hydrolysis.

The postulated transpeptidation reactions leading to the interconversion of α-peptides by either carboxyl or amine transfer reactions (type *d* in the scheme) might prove to be closely connected with protein synthesis, since they would provide a mechanism for re-arrangement of amino-acid residues in α-peptide chain structures. Underlying this suggestion, we have had in mind from the beginning the possibility that the different proteolytic enzymes, with their sharply defined specificity characteristics, may catalyse such transpeptidation reactions, in addition to the hydrolytic reactions by which they are normally recognized. This would be in accord with the important discovery of Axelrod[28] that phosphatases will catalyse both group transfer as well as hydrolytic reactions. The suggestion that the proteolytic enzymes may catalyse transpeptidations, adumbrated by Lipmann[29] gains support from the recent work of Frantz and Loftfield[30] and especially of Brenner *et al.*[7], who have reported the synthesis of peptides by the action of chymotrypsin upon various esters of amino-acids, this being the result presumably of a carboxyl transfer from ester linkage with alcohol to peptide linkage with amino-acid.

Note added in proof. Since the above was submitted for publication, we have read the recent article (*Yale J. Biol. and Medicine*, p. 263, 1950), by J. S. Fruton, entitled "The Role of Proteolytic Enzymes in the Biosynthesis of Peptide Bonds". Fruton develops speculations regarding the possible significance of transpeptidation reactions which are parallel in many ways to ours. In support of the view that proteolytic enzymes may catalyse transpeptidation as well as hydrolytic reactions, Fruton gives evidence that a small but significant amount of isotopic ammonia is incorporated into benzoylglycinamide or carbobenzoxy-L-methioninamide under the action of papain. It seems appropriate here to mention that by another technique we have recently obtained

more direct evidence of the existence of transpeptidation reactions involving α-peptides which are catalysed by plant enzymes.

Acknowledgments

We are grateful to Dr. E. Friedmann for valuable advice in the use of N-ethyl-maleimide and for supplying this compound. Our thanks are also due to Dr. F. Sanger for advice and assistance in the end-group determination.

One of us (F. J. R. H.) held a Sir John and Lady Higgins Research Scholarship (awarded by the University of Melbourne) when this work was begun. It has been continued under a research grant from the Agricultural Research Council. Support from these two sources is gratefully acknowledged.

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AGRICULTURAL GENETICS

CONFERENCE AT RIETI

A MEETING on agricultural genetics held at Rieti during May 30–June 3, although originally announced as a meeting of the Italian Society of Genetics and Eugenics, proved to be a truly international gathering, with representatives from Sweden, France, Switzerland, Spain, Portugal, Yugoslavia, Great Britain, the United States and Israel, and about two hundred Italian delegates. The opening ceremony was attended by the Under-Secretary for Industry and Commerce and many distinguished national, provincial and municipal officials. The meeting was organised by Prof. Carlo Jucci, of the University of Pavia, who was very largely responsible, by his enthusiasm, energy and wide scientific competence, for its success. The opening address was given by Dr. P. S. Hudson (Commonwealth Bureau of Plant Breeding and Genetics, Cambridge), who represented the headquarters of the Food and Agriculture Organisation, and speaking in Italian on "Genetics and Agriculture in International Organization", described the Organisation's World Catalogue of Genetic Stocks. This is a first attempt on a world scale to organise the collection and maintenance of information and living material of agricultural crop plants of potential value to plant breeders.

The second contribution was a paper by Dr. Å. Gustafsson (Sweden), on "Induced Mutations and the Viability Problem". Here some interesting data were given concerning certain mutants obtained by X-ray irradiation of barley. Many of these were of good viability, and some were fully fertile, so that irradiation clearly has potentialities as a tool in plant-breeding. Carefully controlled comparisons over several seasons gave indications that some of these mutations yield best in the years when the mother variety (in this case Maya barley) does not do so well. Dr. Gustafsson pointed out that this is in contrast with colchicine-induced polyploids, the seasonal yields of which follow those of their mother strains. Some mutant lines gave their highest yields with medium dressings of nitrogen, and were depressed by higher dressings which increased the yields of the mother strains. These and other data seemed to provide excellent demonstrations of the generalization that particular alleles each have their specific physiological optima. Irradiation has given rise to one very early line in barley, and to a line which has straw stiffer than that of any other known variety, and which is now already cultivated to a limited extent in Sweden. A line of white mustard with 4 per cent higher yield and higher mustard content has been selected from irradiated material; but in view of the cross-pollination of this crop some uncertainty is felt as to whether this line has originated as a result of the irradiation. Interesting agronomic comparisons of chlorophyll-deficient mutants in barley were also given. Homozygotes of these are lethal, and in one case the heterozygotes, which gave lower yields than the normal in pure stand, gave higher yields under certain special conditions involving competition with normals in segregating progenies, and this superiority was greatest where competition was most intense. It was also shown that certain spontaneous chlorophyll-deficient lethals in barley, the single heterozygotes of which are in certain characters similar to the normals, are superior in dihybrid combinations, and the interesting view was expressed that such deleterious mutations may have taken a positive role in evolution.

A somewhat similar point of view was expressed by Dr. A. Câmara (Portugal), in an address on "Possible Contributions to Plant Improvement", in which an outline was given of the plant-breeding work in progress in Portugal and the methods employed. These include the artificial induction of mutations and polyploids, and the study of the caryological interrelationships of the species in wheat and other plants and the significance of polysomics.

The second day was devoted to discussion of the improvement of cereals, particularly wheat. Dr. Å. Åkerman (Sweden) outlined the history, organisation and achievements of the Swedish Seed Association at Svalöv. It is estimated that plant breeding and

improved agricultural methods together have led to an increase of almost 50 per cent in the yield of wheat in Sweden, and increases of slightly more modest order in other crops. Attention was early devoted to investigation of the potentialities of special techniques such as the artificial induction of mutations and polyploidy. The latter technique appears to be most successful in crops which are grown for their vegetative parts, since fertility is usually depressed. Useful polyploid strains of alsike, red clover and winter rye are already available, and barley, rye, wheat, timothy, mustard, turnip, mangolds and sugar beet show promise. The importance was stressed, in all methods of breeding, of undertaking selection work on a sufficiently intensive scale, and of adequate facilities for field tests over a wide range of conditions. In connexion with the urgent problem of breeding a more winter-hardy wheat, resistance to winter damage by *Fusarium*, *Typhula* and other pathogens is of importance; laboratory methods of testing cold-tolerance were described, and the importance of preliminary hardening was stressed. Old land races are strongly winter-hardy but deficient in all other respects. Yield of winter wheat has been increased 70 per cent during the past fifty to sixty years, and half this increment is due to breeding. Baking-quality was not at first adequate, but, as Sweden became self-supporting in wheat, interest was taken in this feature, and Sweden can now obtain fully satisfactory baking flour by the blending of domestic winter and spring wheats. The contribution of the plant breeders to yield-increase in the spring wheats is estimated at a little more than 20 per cent.

In oats, of which only spring varieties are grown in Sweden, the important observation has been made that yield is not necessarily closely correlated with maturity class. Yield increments of 10–20 per cent are attributed to the breeder.

A short reference was made to oil plants. Cultivation of these was resumed in 1940 as a contribution to the supply of fats in the national diet. They now occupy an important place in the economy of the country, and their cultivation is being maintained, 170,000 hectares having been grown last year. The important oil crops are rape, white mustard and linseed. In addition to straightforward selection for winter hardiness, work is proceeding with polyploids and with interspecific crosses, the latter especially in the genus *Brassica*. Tetraploid types of all species groups of this genus have been obtained; but their vigour is in no case greater than that of their parent types, and often lower. The high-chromosome number species have been artificially synthesized, and these now offer a possibility of introducing winter-hardiness into rape. Progress has been made in improving the fertility of synthetic species through selection. Finally, Dr. Åkerman gave a brief description of provisions for testing, multiplying and distributing improved seed.

Dr. O. Gasparini discussed problems in connexion with seed production in Italy, and Dr. V. Boceta described some interesting results obtained in Spain with maize hybrids produced by crossing plants selected from consanguineous lines, a method which produces notable improvements in less time than that required for the selection of inbreds.

Dr. A. Dionigi described the work of the Nazareno Strampelli Cereal Research Station at Rieti, and the new direction it has taken since the death of the famous breeder, N. Strampelli, former director of the Station. The method now employed consists of making large numbers of crosses (two thousand or so have been made this year) and subjecting the hybrid material to preliminary testing under artificial conditions of environment—for example, in cold chambers at 4° C. for varying periods—before testing them in the field. It was explained that varieties even with the same maturity-period differ in the length of their various developmental phases, and that the treatment permits analysis of these phases and hence facilitates the selection of lines adapted to particular environmental conditions (elevation, cold, humidity, rust prevalence, etc.). It is claimed that, by subjecting segregating progenies to cold-chamber treatment, types can be selected which have developmental phases which are known, from experience and from comparison with standard varieties, to be suitable for particular conditions.

Dr. G. W. Adriance (United States) spoke on "Fruit Breeding Problems in Texas", mentioning especially the production of peaches with a low degree of cold-requirement and capable of giving fruit in Texas, where the winters are often so mild that the common peach varieties cannot be grown. Mild-winter tolerance was derived from the Chinese honey peach, which is not of the best quality and was therefore crossed with commercial types. Mention was also made of work with raspberries, figs and grapefruit. In connexion with the latter, he directed attention to the use of nucellar seedlings to screen out virus diseases, and as a means of rejuvenation of the variety.

Dr. Chanan Oppenheimer (Israel) spoke on fruit-breeding problems in Israel. He referred to the difficulty of growing apples, which suffer damage to blossom through lack of shade during the very hot days of early spring at a time when the trees are still leafless. Pollen-sterility and differences in time of flowering make hybridization with a small-fruited, locally adapted type difficult, but crosses with European types have been obtained, and these in later generations show transgressive segregation for time of leafing. Dr. Gustafsson recommended X-radiation of European types in an attempt to induce bud-mutations which might well be expected to include precocious leafing types.

Dr. A. Morettini presented a useful outline of the fruit-breeding work that has been done in Italy. Special mention was made of the achievements of Pirovano, who as the result of a half-century's labour has produced many excellent varieties of table grapes, some of them possessing special characters, such as a rose flavour or seedlessness, and others possessing new combinations of desirable characters such as high yield, earliness and large fruits. Valuable varieties of pears and peaches produced by Pirovano were also mentioned. Dr. Morettini then described his own work at Florence in producing improved varieties of peach, plum, pear and apple. Attention has now been turned also to the Japanese persimmon. Among the activities of other workers, special mention was made of the discovery at Acireale in Sicily of lemon varieties resistant to the die-back disease (*mal secco*). He stated that the genetic aspects of fruit-breeding have received little attention in Italy and that much requires to be done, especially on such characters as keeping-quality and transportability in relation to export requirements. He made a special plea for further support of such work, including the establishment of a fruit genetics research institute.

Dr. M. Marinucci discussed the problems of olive-breeding in Italy, pointing out the need for a funda-

mental attack from the genetic angle even though this should take centuries to complete. The existing varieties, of which there are many, all have some defect or other, and improvement in such features as drought- and cold-resistance would lead to great increases in production. Examination of further material from the centre of origin was strongly recommended. Studies on floral biology are important in the search for self-compatible varieties. Particular mention was made of work being carried out under Dr. Marinucci's direction at Perugia, where studies of respiration and glycolysis in different combinations of stock and scion have shown which combinations are the most favourable. Differences have been observed even between reciprocal combinations, expressing the different capacities of the respective varieties to utilize raw materials. In the discussion, Dr. R. Ciferri gave his views on the evolution of the cultivated olive, which seems to have been by a process of introgressive evolution, the hybrid evolved by a process of continued backcrossing with one parent, while the other parent of the original cross has disappeared. To what extent modern concepts of species variability had been taken into account in formulating this hypothesis was not clear.

Dr. G. Dalmasso outlined the history of vine-breeding from the pre-phylloxera period to the present day. Interesting points that emerged were that whereas French and German breeders had been almost completely preoccupied with attempts to achieve the hitherto unattainable goal of the direct-producer hybrid, in Italy the two Pirovanos, father and son, had gone ahead with improving the quality of the available material within the European grape species, and so attained the excellent series of varieties now available for grafting on to resistant stocks. Similar activities were carried on at the Viticulture Station at Conegliano under the direction of Dr. Dalmasso himself. He now considers, however, that it may well be profitable at this stage to re-examine the German method of approach, experience having shown that certain resistance genes do exist in the European vines, and by using large numbers of hybrids in advanced generations it is possible that the ideal direct-producer may yet be achieved. He further pointed out that, with the present knowledge of the laws of plant distribution, it is still possible that further collecting expeditions in America might reveal the existence of species capable of giving resistant hybrids of high quality.

The fourth day was devoted to grassland problems. The first contribution was by Dr. F. Marschall (Switzerland) on "Plant-Sociological Considerations regarding Alpine Pastures", in which it was shown that alpine plant species exist in many different and quite definite races, and that the classification of the associations is much more complex than has been supposed. A thorough study of these associations from the plant sociological point of view will undoubtedly help in selecting genetically suitable forms.

Dr. T. J. Jenkin, speaking on "Genetic Problems in the Breeding of Forage Grasses", described the work of the Welsh Plant Breeding Station in evolving strains of pasture grasses of greatly improved persistency and quality. By blending appropriate basic strains carefully selected for known characteristics, mixtures suitable for almost all sets of growing conditions in the British Isles can be obtained. Attention is being devoted to the production of special types for silage and grass-drying.

Interesting views were expressed concerning the evolution of the British strains of *Lolium perenne* from the annual *L. rigidum* of the Mediterranean. Though it has changed in very many genes and gene complexes, it is still not so completely adapted as to survive out of cultivation. On the other hand, *Festuca*, which has evolved by polyploidy, has produced species capable of surviving under ecological conditions other than those to which the parental species are adapted. This should be borne in mind in judging artificial polyploids, which may be inferior in the parental area but yet prove superior in an area outside the range of the parents.

Dr. G. Haussman (Lodi), in a paper on "Problems of Forage Plant Selection in Relation to the Fertility Potentialities of the Soil", laid special stress on the capacity of different plants to influence the soil structure, owing largely to differences in the type of root system they produce. Selection for the types most effective in this respect will contribute materially towards improving the quality of the swards and raising the production capacity of the land.

Dr. M. Mendizábal (Spain) described the work of the agricultural experiment station for arid zones at Almeria, the main problems of which are to find plants capable of growing under conditions where the mean annual rainfall is only 200 mm.

Dr. F. d'Amato (Pisa) gave an account of experiments in which 'Gammexane' was shown to have certain advantages over colchicine as a polyploidizing agent, especially in its low toxicity; it is effective over a very wide range of material. Dr. T. Castelli (Perugia), after giving a review of Winge's work on the genetics of the yeast fungi, reported some observations of his own in which a close correlation between spore form and fermentation capacities was demonstrated.

The final session on the fifth day was held at the Pontifical Academy of Sciences in the Vatican City. Dr. R. Esteruelas (Spain) reported on the work of the Aula Dei Agricultural Experiment Station near Zaragoza, where the activities, all directed towards improving the local crops, are divided into plant-breeding, cytology, ecology, phytopathology and physiology.

Dr. R. Téllez (Spain) referred to difficulties in applying the present systems of classification of wheat species and varieties to a large collection of agricultural varieties, and proposed that a meeting of interested parties should be organised at the next International Genetics Congress in Rome. The meeting unanimously agreed with this proposal.

One of the evening sessions was devoted to a visit to the projected Apennine Research Centre, to be operated jointly by the University of Pavia and the National Research Council. This Centre is a development of the work of Prof. Carlo Jucci in this locality during the past fifteen summers. It is situated in isolated country and with a magnificent outlook at an elevation of 1,730 metres on Monte Terminillo, a few miles from Rieti. The laboratories, in a converted barracks, are nearing completion, and are intended for general biological studies in the fields of taxonomy, cytology, histology, phytopathology and physiology. Particular emphasis will be given to studies in botanical evolution and adaptation on much the same lines as those followed by Jens Clausen and his co-workers at Palo Alto in California. Prof. Jucci hopes also that this will become an international study centre.

OBITUARIES

Dr. Fabius Gross

THERE was something unusually attractive about Dr. Gross; it was partly his self-confidence, bred of knowledge and hard experience, but more his charm of manner, his friendliness and his unfailing good humour in every situation, and not least the catholicity of his sympathies, in the arts as well as in the sciences. He was born in Krosno in 1906, when that town was still in Austria, and at the University of Vienna he studied biology under a distinguished group of teachers, Profs. Storch, Versluys, Przibram, Joseph and Wettstein. As a student he showed aptness for research, recognized by his association with Storch in investigations of the feeding mechanism of Crustacea and the biology of dragon-flies, and his own D.Phil. thesis (1929) was an analysis of the swimming movements of Cladocera based upon microscopic studies with cinéfilm. Three further years of research, on *Artemia* and *Noctiluca*, were spent with Prof. Hartmann at the Kaiser-Wilhelm Institut in Berlin, and then the rising tide of anti-Semitism drove him from his own land to seek shelter in Britain.

There, with the aid of the Academic Assistance Council, he was able to continue his studies—with Huxley at King's College, London, on regeneration in *Sabella* and mitosis in *Artemia*, with Fisher at University College on *Artemia*, and with Allen at Plymouth, where he commenced a promising line of investigation on culture methods for marine Protozoa which led to a study of the neglected micro-plankton and to a recognition of their importance as a basic food-supply for the larvæ of fishes and other marine animals. In 1937 he was appointed lecturer in experimental zoology in the University of Edinburgh, and for twelve years he shared in the work of the Zoology Department. Without previous experience of teaching he became a most stimulating teacher, careful in preparation, constantly devising and testing new experiments with his classes, and guiding his students towards reliance on their own observations rather than on the dogma of text-books.

Meanwhile, Gross continued his own researches, and the originality of his work was acknowledged by the first award of the Jacobsson Fellowship of Sweden, which enabled him during the summer term of 1939 to assist Prof. Hans Pettersson in inaugurating the use of the unique plankton-well in the new Oceanographic Institute of Göteborg. His work on this new venture, then and during a second visit in 1947, was greatly appreciated and admired by his co-workers in Sweden.

In 1940, with more recent refugees, he was interned under the Enemy Aliens Act; but he returned without rancour, and set about planning a series of experiments to test the effects upon the growth of fishes of adding ordinary chemical fertilizers to enclosed or partly enclosed arms of the sea. These experiments, financed by Imperial Chemical Industries, Ltd., were carried out by teams of scientific workers from the Edinburgh Zoology Department and Millport Marine Station, and the final reports on this, an important exploratory contribution to a new outlook on fishery research, appeared only a few days after Dr. Gross's death. He spent the summer vacation of 1949 at Woods Hole Oceanographic Institution, and had not long left Edinburgh to take up the important post of director of the Marine Biological Station to be created at Bangor for the University of Wales, for which he was eminently fitted, when symptoms of serious illness showed themselves; after a characteristically brave struggle he died in Edinburgh on June 18 and was buried there with Jewish rites on the following day.

JAMES RITCHIE

Dr. J. R. Ashworth

SCIENTIFIC societies in the north-west of Britain sustained a great loss on July 9 through the death of Dr. James Reginald Ashworth, of Rochdale. He had only recently resigned from the office of honorary secretary of the Rochdale Literary and Scientific Society, after sixty-five years, and he had been a co-opted member of the Public Libraries, Art Gallery and Museum Committee of Rochdale for sixty-three years. At the age of eighty-nine he had been an influence in Rochdale's cultural life long before many of those who now have to sustain it were born.

In 1893, two years after the Rochdale Technical School was built, Dr. Ashworth was appointed teacher of evening classes in magnetism and electricity and also in heat, light and sound under the old South Kensington scheme for science and art classes. At that time the teaching of physics was not general, except in colleges and universities; much work was therefore necessary in devising experimental courses, which were embodied in two practical text-books written by Dr. Ashworth. In the first year of his appointment, only twenty-three students attended the physics and electrical engineering courses, but when he retired in 1928, the number had risen to three hundred.

In the wider scientific world Dr. Ashworth built up a considerable reputation. He wrote eighteen books and pamphlets dealing mainly with various aspects of magnetism. Recognition of his authority on this subject was made in May 1939, when he was invited to address a conference on magnetism organised at Strasbourg by the French Central Council of Scientific Research.

Dr. Ashworth had also devoted much attention to the study of ultra-violet rays and their relation to sunspot frequency, and only a few months ago he published a small book on this subject, through the Liverpool University Press, based on his own daily observations over a period of sixteen years. He made a number of contributions to *Nature*, mainly on magnetism and also on atmospheric pollution and its effect on the transmission of ultra-violet radiation. For many years he had been deeply interested in the subject of atmospheric pollution. He installed a gauge on the roof of the Rochdale Technical School and made daily observations to the Smoke Abatement Society. He was a fellow of both the Royal Meteorological Society and of the Physical Society.

At the time of his death Dr. Ashworth was curator of the Manchester Literary and Philosophical Society. Up to the end of last year he was in good health, attending the Council meetings regularly and giving valuable advice. He recently presented the Society with a portrait of Joule, whose connexion with the old building in George Street, Manchester, is well known.

The Vicar of Rochdale (the Rev. G. E. N. Molesworth) pays the following tribute to Dr. Ashworth: "He said he valued above all things integrity and truthfulness of heart and mind. So indeed his life has proved. We shall not see his like again and we shall be immeasurably the poorer for it. He has reached the end honourably and unfalteringly with his finger on the pulse of passing events."

Dr. Ashworth was unmarried. He is survived by his elder brother, the Rev. G. H. Ashworth, of Cleadon, Sunderland, and his sister, Miss M. L. Ashworth, of Hindhead, Surrey.

Mr. Thomas Lewis

Mr. Thomas Lewis, head of the Department of Applied Mathematics in the University College of Wales, Aberystwyth, died suddenly on July 6, at the early age of fifty-two. He had not been in good health for some time, but had appeared to be improving. His passing was a great shock to his colleagues at Aberystwyth, who had enjoyed his society only the day before.

Lewis was born at Newport, Pem., and attended the Cardigan County School. After service in the First World War, he entered the University College of Wales, Aberystwyth, in 1919, where he gained first-class honours in applied mathematics, and various University prizes and scholarships. He studied mathematics abroad at Cologne, Bonn and Zurich, coming under the influence of Weyl, and returned to Aberystwyth in 1925 to become assistant lecturer in, and in 1933 head of, the Department of Applied Mathematics. I first met Lewis when giving a course of lectures at Aberystwyth in 1933 on "World-Structure". He took a great interest in the subject of kinematic relativity, and in 1935 published (in the *Phil. Mag.*) a paper in which he suggested that the then unknown form of the acceleration function $G(\xi)$ in the equation of motion of a free particle in the presence of the substratum was probably $G(\xi) \equiv -1$; and he integrated the equations of motion on that hypothesis. Ever since then, he maintained an intermittent correspondence with me on these problems; and only in April last he sent me some notes on the dynamics of the photon and the secular variation of Planck's 'constant' h, which were of considerable interest though incomplete. Lewis also wrote on more conventional electro-dynamics, in particular on Dirac's theory of the world-line of an electron. He was also interested in fluid motion. In all his publications he showed great independence of outlook and fertility of invention. He was also interested in the philosophical implications of modern science, and wrote thereon in Welsh publications.

He is survived by his wife, three sons and two daughters. He will be greatly missed by the Bethel Welsh Baptist Church, and other circles of Welsh culture.

E. A. Milne

NEWS and VIEWS

National Research Council (Canada): Dr. E. W. R. Steacie, O.B.E., F.R.S.

Dr. E. W. R. Steacie, director of the Division of Chemistry of the National Research Council of Canada, has been appointed vice-president (scientific) of the Council. In this new post, Dr. Steacie will be responsible for all scientific activities in the Council to ensure that the work of the several divisions proceeds according to a general plan and to maintain the closest integration of research throughout the laboratories. Dr. Steacie will continue as director of the Division of Chemistry, an appointment which he has held since 1939. During the Second World War he was deputy director of the British–Canadian Atomic Energy Project. He is forty-nine years of age.

Philosophy at Birmingham: Prof. A. B. Gibson

Prof. A. Boyce Gibson, of the University of Melbourne, has been appointed to the chair of philosophy in the University of Birmingham. He is already well known in Birmingham, having been a member of the philosophy staff from 1927 until 1935, and his many friends will welcome his return. The son of Prof. W. R. Boyce Gibson, whom he succeeded in the chair in Melbourne, he was educated in the University of Melbourne and in Balliol College, Oxford. He was temporary assistant in philosophy in the University of Glasgow during 1923–25, and staff tutor to the Joint Tutorial Classes Committee of Oxford in North Staffordshire during 1925–27, where he threw himself wholeheartedly into the movement for adult education. His book on the "Philosophy of Descartes" was published in 1932. Other publications include "Should Philosophers be Kings?" (1939) and (with A. A. Phillips), "Thinkers at Work" (1946). A 'Greats' man and an idealist, he has a deep admiration for Plato. His special interests include political theory, æsthetics and philosophy of religion. The honorary degree of D.Litt. was conferred on him by the University of Cambridge in 1948, when he was in Great Britain as a delegate to the Conference of the Universities of the Empire.

Soil Survey of Great Britain

Soil surveys were started in Great Britain nearly forty years ago; but not until after the First World War, when their use to the agricultural advisory services was realized, were any definite plans made for their development, or soil mapping put on a systematic basis. Since then, standard methods have been gradually built up, activities have been co-ordinated, and in 1939 the Soil Survey of England and Wales attained formal recognition. The general scientific supervision of the work is carried out by the Soil Survey Research Board, which has now issued its first report under the ægis of the Agricultural Research Council (pp. 27; London: H.M. Stationery Office, 1950; 1*s.* 6*d.*). This publication includes some account of the methods used and details of the areas surveyed during 1946 in England and Wales, and Scotland. Mapping is normally made on the scale of 6 inches to the mile; but a considerable amount of reconnaissance work has been done on the 2½- or 1-inch scale. The soils are classified into series, that is, those showing the same general profile characters and developed from the same or similar parent materials. So far, surveys have been almost entirely confined to agricultural soils, as the work is closely linked with the advisory service; but the general value of the work is evident, for, besides being of interest in itself, a knowledge of soils is also important for forestry and in all matters pertaining to land use.

Marihuana in Latin America

Dr. Pablo Osvaldo Wolff, a member of the Expert Committee of the World Health Organisation on Habit-forming Drugs, has written a valuable pamphlet entitled "Marihuana in Latin America, the

Threat it Constitutes" (pp. 56; Washington 6, D.C.: Linacre Press, Inc., 1949; 1.50 dollars), and nobody who reads it can remain in doubt of the evil effects of this drug, which is popularly known under the name of hashish, or Indian hemp. Hemp, says Dr. Wolff, has innumerable common names in various countries, and he relates that the hashish of the Middle East, the kif of North Africa (kif being Arabic for tranquillity or peace), the dagga of South Africa, the anascha of the U.S.S.R., the esrar of Turkey and Persia, the marihuana of Spanish-speaking America and the United States, and the maconha of Brazil are all names for the same substance, which has other names as well. Dr. Wolff discusses its uses, general effects, the value of experimental observations made with it, its psychopathic manifestations and relationship to crime and delinquency, the medico-legal problems that it creates and the use of it in the Latin American countries. After reading his pamphlet, it is indeed difficult not to agree with him that, while opium "cures and punishes like a god", there is no reason or excuse for the use of marihuana, which "has been closely associated since the most remote time with insanity, with crime, with violence, and with brutality". A bibliography of eighty-three references adds to the value of this pamphlet, which presents its facts so vividly and yet in language which everyone can understand.

East African Industrial Research Board

THE seventh annual report of the East African Industrial Research Board (Nairobi: 1*s.* 6*d.*), now operating under the East African High Commission, covers the year ended December 31, 1949, and records that investigations have largely been concentrated on projects already receiving attention. In the field of ceramics, much effort was given to the development of a clay glazing technique for domestic pottery which might lend itself to the production of decorated ware for markets overseas, and steps were taken towards the establishment of the export of high-grade refractory products. Work on bricks and roofing tiles continued, and a suggestion for bonding a natural diatomite, unfired block with sisal fibre for the production of insulating slabs has been adopted commercially. Besides supplying fertilizer by calcining rock phosphate and soda ash for field trials throughout East Africa, laboratory work on the composition of the product continued, as well as the study of the making of bricks from this mixture. Laboratory work on the extraction of pyrethrins from fresh flowers was completed, and some work carried out on the storage of fresh flowers and the so-called 'fermentation' of closely packed flowers, the analysis of undried flowers and the loss in dry material in drying pyrethrum flowers.

National Foundation for Scientific Research, Belgium

THE twenty-second annual report of the Belgian National Foundation for Scientific Research covers the year 1948–49 (pp. 185; Brussels: Fonds National de la Recherche scientifique, 1949). The scientific activities of the Inter-University Institute for Nuclear Physics have included photographic plate technique and cosmic ray studies, the separation of isotopes by thermodiffusion in the liquid phase, the preparation of uranium oxide, the metallurgy of uranium, preparation of pure graphite, geological applications of radioactivity, technique of thin photographic emulsions, preparation of fluorine and uranium hexafluoride, mass spectrography, nuclear isomerism, investigations on the secondary ionization caused by a stream of slow neutrons, and arrangements for obtaining very high temperatures. A report is included on the distribution of radioisotopes in Belgium and also on work during 1948–49 at the Jungfraujoch Scientific Station, under Prof. M. Morand. This has dealt with cosmic rays and the nuclear reactions they produce in photographic plates and has included the study of the essential properties of neutrons and protons of energy greater than that which can be attained with the most powerful cyclotrons or other generators. In addition to details of the membership of the various scientific committees, the report includes an analysis of the distribution of research grants made since the establishment of the Foundation and a list of the national research centres. Lists of recipients of grants, totalling 3,250,000 francs, during the year 1949–50 and including the research objectives are appended, together with a list, by recipients, of publications during 1948–49.

National Central Library, London: Annual Report

THE thirty-third annual report of the executive committee of the National Central Library (pp. 32; London: National Central Library, 1950) covers the year ended February 28, 1949, and records a smaller total increase of 10·43 per cent in the issues of books from or through the Library to all categories of libraries which it serves. Total issues were 93,745 as against 84,889 in 1947–48, and, of these, 10,445 were to or from university libraries, 695 to or from Imperial or foreign libraries, and 9,405 to or from the libraries of government departments, research and industrial organisations, etc. Issues from the Scottish Central Library for Students were 15,717, as against 15,547 in 1947–48, and from the Irish Central Library for Students, 12,873 as against 13,082, while total issues of the adult class department, the stock of which was augmented by 3,584 volumes, increased from 12,652 in 1947–48 to 18,123. Reference is again made to the value of the Bureau of American Bibliography as a source of information about American books and periodicals, and to the increased assistance given by the outlier libraries, which lent 17,926 volumes during the year compared with 15,023 in the previous year. Work has progressed steadily on the union catalogue of books in the Russian languages in libraries in the United Kingdom, and compilation of a union catalogue of all German war-time periodicals held by British libraries has been commenced. There are arrears of approximately 443,000 entries still to be incorporated in the National Union Catalogue, but work has proceeded on the Union Catalogue of outlier libraries, and entries contributed to Union Catalogues total 3,639,963 at the National Central Library, 885,181 in Wales, and 140,278 in Scotland. During the earlier part of the year, the British National Book Centre was still engaged largely in disposing of the remaining stocks of books and periodicals transferred in December 1946 from the Inter-Allied Book Centre, but later the staff proceeded to make systematic arrangements for its main task of co-ordinating the exchange of redundant material within Great Britain and between Britain and other countries. The Treasury grant-in-aid was increased from £14,500 to £19,000, including a sum of £1,000 to compensate for the first stage in the discontinuance of the contribution from the Carnegie United Kingdom Trust.

Australian Journal of Marine and Freshwater Research

A NEW scientific periodical, the *Australian Journal of Marine and Freshwater Research*, has been established by the Commonwealth Scientific and Industrial Research Organisation as a medium for the publication of research papers on the results of original investigations on sea, estuarine and freshwater fisheries and cognate subjects. Dr. N. S. Noble, of the Organisation's staff, has been appointed as editor of the new *Journal*. He will have the help of an Editorial Advisory Committee including Mr. G. Humphrey (Department of Biochemistry, University of Sydney), Prof. P. D. F. Murray (Department of Zoology, University of Sydney) and Dr. H. Thompson (Chief, C.S.I.R.O. Division of Fisheries). The *Journal* will not be issued at set periods, but as the accumulation of suitable material dictates. It is possible, however, that two issues will appear each year. The subscription rate is A.7*s*. 6*d*. per issue. Further information can be obtained from the Secretary, C.S.I.R.O., 314 Albert Street, East Melbourne, C., Australia.

Documentation of Architecture and the Building Industry in Italy

A NEW quarterly, *Documenti di Architettura e Industria Edilizia* (Centro Studi Abitazione presso il Consiglio Nazionale Ricerche, Piazzale delle Scienze, 7 Rome; home, 1,800 lire; foreign, 3,600 lire a year), is, for the most part, a production inspired and guided by the Building Documentation Conference held in Geneva in October 1949. Part 1 consists of abstracts from the Italian literature, in boxes, eight to the page (each size *A*7), with the Universal Decimal Classification numbers on the top right corner. On one side the abstract is in Italian for domestic use, while on the back it is in French for international use; the abstracts may thus be cut out, attached to cards and filed by the Universal Decimal Classification. Parts 2–5 consist respectively of: selected foreign abstracts (in Italian for domestic use); data sheets (in Italian and French) of the form introduced in 1948 by the Bouwcentrum, Rotterdam, in which a building is described in detail with photographs, plans and elevations; reviews of foreign literature (in Italian); and an outline of standards relating to buildings in one or more foreign countries. By this publication there is made available to the building industry all over the world a complete analysis of the relevant Italian literature already abstracted and classified. As the first national publication of its kind, it is a model example for others to follow. Seventeen countries have agreed to publish similar abstracts, and the realization of the full international scheme will have a very great effect in promoting co-operation in building industry research, as well as pointing the way to the solution of similar problems in other industries.

President Truman's Fourth Point

THE Fourth Point in President Truman's inaugural address of January 20, 1949, called for a "bold new program for making the benefits of our scientific advances and industrial progress available for the improvement and growth of undeveloped areas". According to the March volume of the *Annals of the American Academy of Political and Social Science*, which contains a valuable symposium on "Aiding Undeveloped Areas Abroad", this Fourth Point is becoming one of the most discussed features of United States foreign policy of the present day. Briefly, the proposal is that the United States should make available its technical knowledge to those living in undeveloped areas, who then, by combining their own resources with 'know-how', may be enabled to improve the conditions under which they live. This is supplemented by the further proposal that capital investment in areas needing development should be fostered on a joint basis. Nineteen contributors have been enlisted by the editor of the *Annals*, each a leading authority on the topic, and the symposium covers the objectives of the programme, the international environment to which it applies, the existing means of putting the programme into effect, and some of the results which reasonably may be expected. A considerable measure of agreement has been achieved by the contributors, despite the diversity of their backgrounds and the so far largely unformulated character of the programme. Though not unaware of the obstacles in the way of application, they see in the programme an important feature of the United States foreign policy.

Effect of Musical Accompaniment to Educational Films

IT is important for teachers and educational film makers to know the conditions for obtaining the maximum attention for the visual element in films. An investigation made by Mr. C. Denis Pegge, of the Cambridge University Educational Film Council, provides evidence that musical accompaniment to 'silent' films aids attention. During the course of film sessions given in the regular teaching time-table of second-year engineering students, a film session was arranged to allow accompanied and unaccompanied 'silent' films to be compared. No indication was given beforehand that this film session would differ from the others, and during the showing normal procedure was so far as possible followed. Each film lasted about ten minutes. The music was of low volume, by Litolff and Raff. The first film was projected without, and the second with, accompaniment. The students who thought music had aided their attention were 52, those who thought it had hindered attention were 2, and those who thought it made no difference were 5. The third film was then projected with accompaniment and the fourth film without. Judging by all four films seen, the students who thought music aided attention were 42, those who thought it hindered attention were 5, and those who thought it made no difference were 13.

Indo-Pacific Fisheries Council: Second Annual Meeting

THE Indo-Pacific Fisheries Council held its second annual meeting at Cronulla, New South Wales, Australia, during April 17–28. The meeting was attended by thirty-five representatives of eleven of the fourteen member governments of the Council. Representatives were also present from the Supreme Command of the Allied Powers (in Japan), the United Nations Educational, Scientific and Cultural Organisation and the South Pacific Commission. The Council elected Dr. J. D. F. Hardenberg, of Indonesia, as its chairman, and Dr. D. V. Villadolid, of the Philippines, as vice-chairman for 1950–51. Technical committees were appointed, and various *ad hoc* sub-committees were set up. Technical Committee I, which deals with biology and hydrology, proposed to do work on the tunas and on the neritic–pelagic group

of fish, and will carry out studies on fish culture, the transplantation of fish, planktology, hydrology and taxonomy; Mr. W. H. Schuster, of Indonesia, was appointed chairman, and Mr. G. W. Rayner, of Australia, *rapporteur*. Technical Committee II, which is concerned with technology, economics and statistics, will continue its programme of surveying the industries of the Indo-Pacific region; Mr. Claro Martin, of the Philippines, was appointed chairman, and Mr. C. G. Setter, of Australia, *rapporteur*. A number of technical papers covering a wide range of activities were received by the Council, and the Committee sent in reports submitting recommendations and resolutions for future work. One of the major projects of the Council consists of a register of the projects, institutions, vessels and personnel concerned with fisheries work in the Indo-Pacific region. Plans have been made for the completion of this register and for its publication at the earliest opportunity.

Guide to the Pharmacy of Poisons

Only a small proportion of scientific workers have to deal with poisons; but those who do will be glad to have the fifth edition of the "P.J. Poisons Guide" (pp. 46; London: Pharmaceutical Press, 1949; 3*s*. 6*d*., interleaved 4*s*.), which contains a great deal of valuable information. It summarizes the Pharmacy and Poisons Act, 1933, giving lists of substances included in its four schedules, and also the Pharmacy and Medicines Act, 1941. These summaries are followed by an extended list of poisons and substances containing poisons, with an indication of the special restrictions applying to each. The fifth, eleventh, twelfth, thirteenth and fourteenth schedules to the poisons rules are also reproduced.

Precautionary Measures against Toxic Chemicals used in Agriculture

The Minister of Agriculture and Fisheries has appointed a working party on precautionary measures against toxic chemicals used in agriculture. Its terms of reference are: "To make recommendations for the promotion of the safety of workers in the agricultural use of substances which are toxic or harmful to human beings: and in particular to advise on the recommendations on this subject made in the Report of the Gowers Committee on Health, Safety and Welfare in non-industrial Employment". The membership of the working party is as follows: Prof. S. Zuckerman (*chairman*), Mr. A. B. Bartlett, Dr. R. A. E. Galley, Mr. C. T. Gimingham, Mr. A. Holness, Mr. W. Morley Davies, Mr. R. G. C. Nisbet, Dr. J. M. Rogan and Mr. H. Cole Tinsley. The joint secretaries are Mr. K. R. Allen, Office of the Lord President of the Council, and Dr. J. T. Martin, Ministry of Agriculture and Fisheries (Plant Pathology Laboratory).

University of London

The following appointments have recently been made: Dr. Frederick Murgatroyd, to the Wellcome chair of clinical tropical medicine tenable at the London School of Hygiene and Tropical Medicine; Dr. S. D. Elek, to the University readership in bacteriology tenable at St. George's Hospital Medical School; Dr. Bernhard Katz, to the University readership in physiology tenable at University College; Dr. D. S. Rice, to the University readership in Islamic art and archæology tenable at the School of Oriental and African Studies. The title of reader in photoelasticity in the University has been conferred on Mr. H. T. Jessop, in respect of the post held by him at University College, and that of reader in highway engineering in the University on Mr. B. G. G. Manton, in respect of the post held by him at the Imperial College of Science and Technology.

Announcements

By an Order of the Committee of Privy Council for Medical Research, made after consultation with the Medical Research Council and with the president of the Royal Society, Prof. W. E. le Gros Clark, professor of anatomy in the University of Oxford, and Prof. F. G. Young, professor of biochemistry in the University of Cambridge, have been appointed to be members of the Medical Research Council from October 1, and by the same Order Group Captain C. A. B. Wilcock has been re-appointed a member from that date.

Mr. R. L. Fortescue has been appointed senior lecturer in charge of the Particle Accelerator Laboratory, which is under construction at Queen Mary College, London, and which is designed for the study of machines used in nuclear physics and radiotherapy and the principles relating to the use of nuclear energy; since 1945, Mr. Fortescue has been working at the Atomic Energy Research Establishment, Harwell, as a principal scientific officer.

The following officers of the Scientific Instrument Manufacturers' Association of Great Britain, Ltd., have been elected for the year 1950–51: *President*, M. H. Taylor; *Vice-Presidents*, J. E. C. Bailey and A. W. Smith; *Honorary Treasurer*, S. Borthwick; and *Honorary Secretary*, J. Rock Cooper.

The Pharmaceutical Society's research scholarship of £300 a year for two years has been awarded to Miss B. P. Jackson, who since 1947 has been a member of the staff of the Department of Pharmacy, University College, Nottingham (now the University of Nottingham), and of the School of Pharmacy, University of London. Miss Jackson will work in the Museum of the Society on genetical and cultivation investigations of vegetable drugs.

A research fellowship in electrical engineering, to be known as the W. T. Henley fellowship, has been established by Messrs. W. T. Henley's Telegraph Works Co., Ltd., at Queen Mary College, London. The fellowship, which is worth up to a maximum of £600 a year, is for senior research workers who have already had some works experience, and it is hoped that the investigations carried out will be more particularly in the field of dielectrics, high-voltage engineering and arc-interruption phenomena, for which the resources of the College are particularly good.

The publication by the Tin Research Institute, Fraser Road, Perivale, Greenford, Middlesex, at the very low price of 2*s*. 6*d*., of its brochure on the equilibrium diagrams of the tin alloys will be welcomed by all metallographers. It is extremely well produced, the diagrams are adequately large and very clear, while the references will be still further welcomed. Although the diagrams published deal only with the binary alloys, there is a very useful bibliography of the ternary ones. Where the crystal structure of the phases has been worked out, the results are given, together with short notes on discrepancies between the results of different workers.

NATURE AND RELATIONSHIPS OF THE SPECIFIC PRODUCTS OF THE HUMAN BLOOD-GROUP AND SECRETOR GENES*

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THE classical blood-group characters shown by human erythrocytes arise from the presence of substances which are specific gene products, each of which, together with its specific immunological character, arises as if controlled by a single gene. Schiff and Sasaki[1] established many years ago that within the *ABO* classification the presence or absence of water-soluble specific group substances in the tissue fluids and secretions of an individual is controlled by a pair of allelic genes, *S* and *s*, *S* being dominant in effect to *s* and determining the secretion of the specific substance. It would, therefore, be correct to say that the presence of the water-soluble *A*-, *B*- and *H*-substances is controlled by the genes specific for these characters *and* by the gene of secretion, *S*. Those individuals who secrete their blood-group substances in a water-soluble form are termed 'secretors', whereas those who do not secrete these factors or do so weakly are called 'non-secretors'.

The isolation and characterization of these specific substances has been the subject of numerous investigations within the past few years, and it is now believed that the specific blood-group characters are due to well-defined chemical entities known as mucoids, or more precisely as polysaccharide – amino-acid complexes[2].

The soluble material secreted by group *O* persons —the so-called *O* substance mentioned so frequently in the literature—is not a specific product of Bernstein's *O* gene[3]. This substance is secreted by individuals belonging to all groups within the *ABO* system, not excluding group A_1B. According to Bernstein's theory, the latter genotype cannot possess an *O* gene. For reasons which have been described in detail elsewhere, this so-called *O*-substance is better called *H*-substance, to indicate its heterogenetic character and to show that it is a common secretion of the great majority of persons who are 'secretors', irrespective of their *ABO* group[4]. The erythrocytes and secretions of persons who possess anti-*H* agglutinins in their sera show no capacity to react with this iso-agglutinin.

A new human blood-group character called 'Lewis' was described a few years ago by Mourant[5], who found that the red blood cells of about 25 per cent of English people are agglutinated by anti-'Lewis' sera and that the agglutination is independent of the other known blood-group characters (*ABO*, *MN*, *Rh*, *P*, Lutheran and Kell systems). Andresen[6] in Denmark observed that anti-'Lewis' serum agglutinates the erythrocytes of about 75 per cent of Danish children who are less than six months old, and that parents, the red cells of both of whom fail to agglutinate with these sera, can have children whose erythrocytes are agglutinated. Andresen concluded that the agglutinability of the erythrocytes of adults behaves as a recessive Mendelian character, that is, adult persons whose red cells possess this agglutinability are genetically homozygous. More recently, Race[7] and his co-workers have found that the results of family studies for the 'Lewis' character strongly support this conclusion.

Two 'Lewis' genes are now recognized and are designated by the symbols Le^a and Le^b, and the corresponding antibodies to the gene products by anti-Le^a and anti-Le^b. If the antiserum, anti-Le^a, is used alone in agglutination tests, the phenotype of the cells which react is defined as $Le(a+)$, those not agglutinated, as $Le(a-)$. Though it has since been shown that the 'Lewis' and *ABO* genes are jointly responsible for certain serological phenotypic characters, the two systems are genetically independent.

It has been found that all persons whose red cells are agglutinated by anti-Le^a serum and who are presumably of the genotype Le^aLe^a are non-secretors of their corresponding *A*-, *B*- and *H*-substances[4]. The close correlation of the agglutinability of adult erythrocytes with anti-Le^a serum—the so-called 'Lewis' positive character—with non-secretion within the *ABO* system is of great interest, and when considered in the light of the finding that 'Lewis'-positive people secrete a water-soluble specific Le^a-substance in their tissue fluids, reveals the fact that the great majority of individuals secrete a blood-group factor and that there are probably no persons who are really 'non-secretors' in the sense of not secreting a blood-group substance. The converse relationship between adult cells which fail to agglutinate with anti-Le^a serum—'Lewis'-negative character —and the secretion of the *ABO* blood-group substances is also very close, but not absolute, and it has been found that possibly about one per cent of all individuals secrete neither *A*-, *B*-, *H*-, nor the 'Lewis' Le^a- and Le^b-substances. It seems probable that this small group of persons are, in fact, secreting a blood-group substance which might well be a product of a third 'Lewis' gene, Le^c. As the corresponding antibody is unknown and the genetics of the 'Lewis' system are not completely understood, it is not possible at the moment to know whether this suggestion is correct.

Here two points of some practical importance might be mentioned. First, a good estimate as to the secretor – non-secretor status of an individual within the *ABO* classification can be made on the basis of a simple agglutination test with anti-Le^a serum. Erythrocytes which show agglutination are derived from persons who are *ABO* non-secretors. The determination of non-secretion within the *ABO* system likewise indicates that the person concerned is most probably 'Lewis'-positive and possesses the Le^a gene in double dose. Less than one per cent of individuals are likely to prove exceptions to these conclusions. Secondly, it may be concluded that in the secretions of an individual, Le^b-substance and *H*-substance (and *A*- and/or *B*-substances if the person belongs to groups *A* and/or *B*) will be found *together*. The biochemical problem of isolating the Le^b-substance as a serologically homogeneous material is likely to be considerably more difficult than that encountered in obtaining Le^a-substance as an essentially homogeneous entity.

* A contribution to a symposium on "Biochemical Genetics" arranged by the Genetical Society and held at University College, London, on March 29.

Table 1 Analytical Figures (average values) for Preparations of the Human Blood-group Substances

	Rotation	Nitrogen	Acetyl	Hexosamine*	Reduction†	Fucose**
	[α]	%	%	%	%	%
A-Substance	+15°	5·7	9·0	37	56	13
H-Substance	−30°	5·3	8·6	31	54	13
Le^a-Substance	−40°	5·0	9·9	32	57	12

* As glucosamine base.
† In terms of glucose equivalent.
** Hydrolysis and periodate oxidation; estimated as acetaldehyde.

The examination of the physical, chemical and serological properties of the *A*-, *H*- and *Le*^{a}-substances shows how very similar they are, and some of the analytical figures obtained for these materials are given in Table 1. The group substances are judged to be essentially homogeneous on the basis of their physical, chemical and immunochemical behaviour. The sedimentation and diffusion constants of the *A*-substance indicate that the particle size of this material is not less than 250,000, and preliminary values of these constants for the *H*- and *Le*^{a}-substances suggest that these materials are of the same order in size. Examined in the Tiselius electrophoresis apparatus at *p*H 4 and 8, the materials migrate slowly towards the anode as a single, well-defined boundary. The inhibition end-points found when the substances are titrated against two to three completely agglutinating doses of homologous and heterologous human iso-agglutinins are set out in Table 2, and show that the amount of heterologous specificity in each material is quite small, certainly less than 1 per cent of the activity shown with the homologous reagent. Each of the *A*-, *H*- and *Le*^{a}-substances yield about 13 per cent of the methyl-pentose, L-fucose, on mild acid hydrolysis, and lose completely their specific group character. At the same time the substances develop or display enhanced reactivity with horse anti-pneumococcus type XIV serum and thus reveal the presence of a common structural unit. The group substances give qualitatively similar amino-acid (eleven amino-acids) and sugar chromatograms, and in each group material there is present, in different proportions, both glucosamine *and* chondrosamine[9]. Finally, the group materials after treatment with alkali under rather special conditions yield, on the addition of Ehrlich's reagent, a bright purple-red colour. This characteristic property, which is due to the extreme alkali lability of an unidentified structure common to all the group substances, has not been encountered during the examination of many other complex mucopolysaccharides and can, until it is found to be otherwise, be considered as a reasonably specific test for the blood-group mucoids or materials closely related to them. It is of interest to report that a further mucoid material, of unidentified blood-group character, has been isolated from the secretion of an individual known to belong to the rare 'Lewis' phenotype *Le*(*a*−*b*−) non-secretor *ABH*, and this material likewise gives this characteristic and apparently specific colour reaction.

It has been observed that all persons who possess Schiff's secretor gene, *S*, have red cells which are not agglutinated by anti-*Le*^{a} serum, and it would appear, therefore, that there is a close, although inverse, relationship between *Le*^{a} and *S* genes. The great majority of the bloods which fail to react with *Le*^{a} serum, however, react with anti-*Le*^{b} serum. It is probable that adult bloods of the phenotype *Le*(*a*+*b*+) do not exist; they have certainly not been observed. It might be anticipated, therefore, that there is some kind of close relationship between *Le*^{b} and *S* genes. A number of specimens of human *H*-substance were tested for their capacity to neutralize each of several specimens of human *H* and *Le*^{b} antibody and the two activities expressed as a ratio. The results suggest that human *H*-substance and *Le*^{b}-substance are not identical, and the detection of individuals of the phenotype *O Le*(*a*−*b*−) secretor of *H*-substance but not of *Le*^{a}- or *Le*^{b}-substance gives further evidence for believing that genes *S* and *Le*^{b} are not identical.

Table 2. Serological Specificity of Human Blood Group Substances. End-Titre of Inhibition against 2–3 Agglutinating Doses of Human Serum

	Anti-*A*	Anti-*H*	Anti-*Le*^{a}
A-Substance	1×10^6	$< 1 \times 10^5$	$< 1 \times 10^4$
H-Substance	$< 2 \times 10^3$	5×10^5	2×10^5
Le^a-Substance	$< 2 \times 10^3$	$< 2 \times 10^3$	1×10^6

Individuals whose red cells are agglutinated by anti-*Le*^{a} serum most probably possess, as stated earlier, the *Le*^{a} gene in double dose, and they are non-secretors of *A*-, *B*- and *H*-substances. Schiff and Sasaki showed that non-secretors within the classical *ABO* system possess the gene of non-secretion, *s*, in double dose. Does the very close correlation which clearly exists between the occurrence of *Le*(*a*+) erythrocytes and non-secretion within the *ABO* system indicate that the genes *Le*^{a} and *s* are identical? A few individuals have been observed of the phenotype *Le*(*a*−*b*−) in whose saliva no *A*-, *B*-, *H*-, *Le*^{a}- or *Le*$_b$-substances are detectable. The existence of such persons makes it improbable that genes *Le*^{a} and *s* are identical.

Is this very close correlation of 'Lewis' character and non-secretion an instance of linkage in man? It is obvious that if *Le*^{a} and *s* genes are linked, the linkage must be a very close one, as in the *Rh* system, otherwise crossing over would obliterate the observed *Le*(*a*+) – non-secretor association in the general population.

It has already been suggested that a close linkage of this kind allows one to place these genes and the genes *Le*^{b} and *S* in one genetic system, and the fact that the physical and chemical properties of the soluble products of these genes, the *Le*^{a}-, *Le*^{b}- and *H*-substances, are very similar might lend some support for this action. As a tentative scheme, therefore, one might consider that there are two sets of allelomorphic genes *S* and *s*, and *Le*^{a}, *Le*^{b} and *Le*^{c} which occupy contiguous loci. The 'Lewis' genes *Le*^{a}, *Le*^{b} and *Le*^{c} are then considered as multiple allelomorphs. A somewhat more complex 'Lewis' system has already been proposed[10].

It has been stated that a series of genes which can occupy the same locus in the chromosome (multiple allelomorphs) have similar functions and produce similar gene products. This being so, it is not surprising that the products of the *A* and *B* genes are basically similar materials. If the so-called *O*-substance (*H*-substance) is not a product of a gene allelomorphic with genes *A* and *B*—and there are reasons for believing it is not—it is perhaps more surprising that this material is so similar chemically to the *A*- and *B*-gene products. Similarly, the genes *Le*^{a} and *Le*^{b}, which are responsible for the development of the 'Lewis' blood-group characters, are on different chromosomes from those which carry the *A*- and *B*-genes, or at least are so remote in position on the same chromosome as to give no evidence of linkage with *A*- and *B*-genes. In spite of this the *Le*^{a} and *Le*^{b} genes give rise to specific substances—the *Le*^{a}- and *Le*^{b}-substances—which are found to possess a type of molecule very similar to the *A*- and

B-gene products. These serologically different complex molecules, all of which seem to belong to a special type of polymolecular aggregate, are characteristic of the water-soluble blood-group substances, and it would appear that there is a common or basic molecular framework which develops minor quantitative, and perhaps qualitative or stereochemical, modification according to the specific action of the gene concerned with its production.

Since genetics is concerned with the innate differences between individuals, the results described above are of immediate interest. The urgent problem is to determine the precise differences in the closely related gene-products discussed. The results of an immunochemical approach along these lines will ultimately express in chemical terms an important aspect of the specific action of the blood-group genes in man.

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SONIC DISINTEGRATION OF ISOLATED LIVER MITOCHONDRIA

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RECENT studies of the biochemical properties of intracellular components isolated from mammalian liver by means of centrifugal fractionation have indicated that the mitochondrion is responsible for a number of important enzymatic processes of the cell. Among the enzyme systems associated with isolated mitochondria are cytochrome oxidase[1,2], succinoxidase[1,2,3], adenosinetriphosphatase[1], octanoic acid oxidase[4,5], oxalacetic acid oxidase[6], and diphosphopyridine nucleotide – cytochrome reductase[7]. It may be noted that all these systems have, up to the present, been refractive to purification and detailed study because of their 'insolubility'. Of the better-characterized proteins which have been obtained from animal tissues in soluble form, only a few, for example, cytochrome *c*[8,9] and triphosphopyridine nucleotide – cytochrome reductase[10], have been found in mitochondria in a concentration exceeding that in whole liver.

Parallel studies relating to the structure of mitochondria, including cytological observations of the behaviour of the isolated particles when subjected to changes in the osmotic pressure of the suspending media[3], have provided evidence for the existence of a well-defined mitochondrial membrane. Although this evidence has been substantiated by electron microscopy[11,12], there remains some question as to the integrity of the membrane, as judged by its ability to retain soluble compounds after the mitochondrion has been released from the cell.

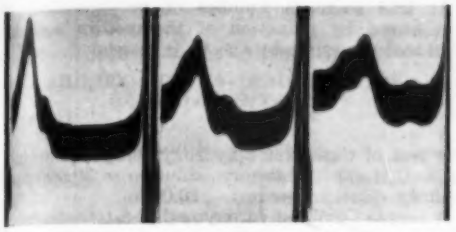
In view of these findings, it was considered of interest to determine whether the activity of several of the complex 'insoluble' enzyme systems is dependent on the structural integrity of mitochondria, and whether mechanical disruption of the mitochondrial membranes would result in the release of a significant amount of soluble material. Preliminary investigations that appear to have a bearing on these problems have been carried out.

Mitochondria were isolated from rat liver homogenates prepared in 0·25 *M* sucrose by a procedure described elsewhere[9]. The final preparation (*M*, cf. table), consisting of mitochondria that had been sedimented three times and resuspended in 0·25 *M* sucrose, was essentially free of nuclei, submicroscopic particulate material, and non-sedimentable nitrogen-containing compounds. The preparation was subjected to sonic vibrations in a 9-kc. per second oscillator (Type *R*-22–3, manufactured by the Raytheon Co., Waltham, Massachusetts) until phase-contrast microscopy revealed relatively few remaining visible particles. During this operation, which required 35–55 min., the temperature was maintained at 2–3° C. The resulting slightly opalescent suspension (M_s, cf. table) was centrifuged for 10 min. at 9,200 rev./min (5,000 *g*) using the multispeed attachment of the international refrigerated centrifuge. The small pellet of residual unbroken mitochondria was resuspended in 0·25 *M* sucrose (Sd_1, cf. table), and the supernatant fluid was centrifuged at 50,740 rev./min. (148,000*g*) for 30 min. at 3° C. in the Type *A* preparative rotor of the Model *E* Spinco ultracentrifuge (Specialized Instruments Corp., Belmont,

Effect of Sonic Vibrations on Enzymatic Activities of Isolated Liver Mitochondria

Preparation*	Total Nitrogen†	Cytochrome oxidase		Succinoxidase		Octanoic acid oxidase		DPN-cytochrome reductase	
	Recovery‡	Recovery‡	Q_{O_2}§	Recovery‡	Q_{O_2}§	Recovery‡	Q_{O_2}§	Recovery‡	Q‖
M	(100)	(100)	9,800	(100)	2,160	(100)	353	(100)	3·50
M_s	98·0	83	8,530	50	1,090	0	0	88	3·20
Sd_1	6·2	7	8,600	5	1,860	0	0	4	1·76
Sd_2	39·0	36	10,400	36	2,200	0	0	46	4·75
S_2	57·7	25	4,350	5	186	0	0	31	1·41

* For explanation of symbols denoting preparations, see the text.
† The average total nitrogen content of the original suspensions of mitochondria (Preparation *M*) was 0·610 mgm. per ml.
‡ Per cent recovered from original preparation of mitochondria (Preparation *M*).
§ Microlitres oxygen consumed per hr. per mgm. nitrogen at 38° C.
‖ Micromoles cytochrome *c* reduced per min. per mgm. nitrogen at 24° C.



Sedimentation of mitochondrial proteins. Protein concentration approximately 2 per cent in 0·06 *M* potassium phosphate buffer, pH 7·4; centrifugal force at centre of cell, 260,000 times gravity; temperature 24° C.; photographs taken at 16-min. intervals; magnification, 1½ diameters

California). The clear yellow supernatant (S_2, cf. table) was removed, and the firmly packed, reddish-brown pellet was resuspended in 0·25 *M* sucrose (Sd_2, cf. table).

The effect of sonic vibrations on the cytochrome oxidase, succinoxidase, octanoic acid oxidase, and diphosphopyridine nucleotide – cytochrome reductase activity of rat liver mitochondria is shown in the accompanying table. Determination of the enzyme activities was carried out as described previously[1,4,7], and each value in the table represents the average obtained in two or more experiments. It is apparent that, although all the enzyme systems were affected to some extent, there was considerably greater inactivation of succinoxidase than of cytochrome oxidase or diphosphopyridine nucleotide – cytochrome reductase. Octanoic acid oxidase was completely inactivated. In additional experiments, the extent of inactivation of succinic dehydrogenase, as determined spectrophotometrically by the rate of reduction of ferricyanide or cytochrome *c* in the presence of cyanide, was essentially the same as that found with the aerobic succinoxidase determination.

Interpretation of the inactivation of enzyme systems occurring when mitochondria were disrupted is rendered somewhat uncertain by reports of oxygen activation by intense sonic vibrations[12], and by the fact that the preparations were exposed to metal (stainless steel) surfaces during the treatment. In this respect, however, it was found that inactivation of succinic dehydrogenase could not be prevented either by the exclusion of oxygen or by protection of the mitochondria from exposure to metal.

Also shown in the table are the amounts of total nitrogen and enzyme activity recovered in the fractions isolated by low- and high-speed centrifugation after sonic disintegration of mitochondria. Of considerable interest is the finding that an average of 57·7 per cent of the total nitrogen remained in the supernatant (S_2) after centrifugation for 30 min. at 148,000 *g*. Moreover, this supernatant contained a significant proportion of the cytochrome oxidase and diphosphopyridine nucleotide – cytochrome reductase activity of the original suspension of mitochondria. Most of the remaining nitrogen and enzyme activity was found in Sd_2.

Experiments were then undertaken to obtain further information concerning the composition of the supernatant (S_2). Of the total nitrogen of the preparation, 97 per cent was precipitated by 1·2 *M* perchloric acid and was insoluble in ethanol; approximately 15 per cent diffused through 'Cellophane' on dialysis for 24 hr. at 2° C. against 0·25 *M* sucrose. In other experiments the supernatant was dialysed against 0·01 *M* potassium phosphate buffer (*p*H = 7·4) until the sucrose was removed, concentrated at 2° C. by placing the 'Cellophane' bag in front of a fan, and studied in the Spinco analytical ultracentrifuge. As shown in the accompanying illustration, there were present at least three components sedimenting at different rates. The observed sedimentation constant for the main component (middle peak in the illustration) was approximately 7·2 Svedberg units; corresponding values for the fast and slow sedimenting components were approximately 12·0 and 4–5 Svedberg units, respectively.

The experiments thus demonstrate that disruption of the mitochondrial membrane is accompanied by the release of a relatively large amount of protein that can be characterized on the basis of rate of sedimentation in the analytical centrifuge. Further investigations of the properties of the soluble proteins of mitochondria will be reported in detail elsewhere.

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MODIFICATION OF AN ANTI-TUBERCULAR MOLECULE

By Dr. VINCENT C. BARRY, J. G. BELTON, ROSE M. KELLY and D. TWOMEY

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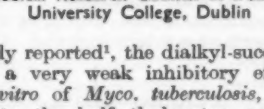
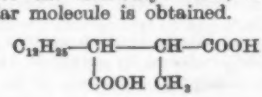
As already reported[1], the dialkyl-succinic acid (I) shows a very weak inhibitory effect on the growth *in vitro* of *Myco. tuberculosis*, whereas on conversion to the half-ethyl ester, a very active antitubercular molecule is obtained.



I



II

The half-ester was prepared from the anhydride of (I) and consists of a mixture of the two possible isomeric mono-esters (*loc. cit.*). The ester (II) preponderates in the mixture, and for the purpose of this study the presence of the isomeric half-ester has been ignored. In the form of the sodium salt, the half-ester inhibits completely the growth of various strains of *Myco. tuberculosis* for six weeks in horse-flesh broth at dilutions between 200,000 and 400,000.

Incorporation of 5 per cent pooled human serum in the broth reduces the inhibitory dilution to 10,000–20,000.

When given orally to guinea pigs experimentally infected with tuberculosis (*H* 37*Rv* strain), at a dosage-level of 100 mgm./kgm. daily for some months, the sodium salt of the half-ester (designated as *B*.53) produced a 20 per cent increase in survival-time. When injected subcutaneously, it produced very toxic local reactions. A dose of 50 mgm. injected three times a week produced a significant decrease in pulmonary disease in experimentally infected guinea pigs. *B*.53 has now been tried in a limited way in the clinic by local application to tuberculous lesions, and it has been shown to produce rapid healing of tuberculous sinuses and ulcers. When instilled *per catheter* in the form of a buffered solution (0·5 per cent), it has eliminated quickly long-standing tuberculous lesions in the urinary bladder which persisted after nephroureterectomy[3].

This partial success encouraged us to attempt, by suitable modification of the *B*.53 molecule, the synthesis of a substance in which high anti-tubercular potency would be preserved, while reducing considerably the antagonistic action of serum, and thus providing a drug which might meet with a better chance of success on systemic administration. This must not be taken as implying that we subscribe to the widely held view that strong antagonism of the action of an antibacterial substance *in vitro* by serum is *always* a sufficient reason for discarding it without trial *in vivo*.

B.53 is a highly surface-active substance producing hæmolysis of washed human red-blood cells in high dilution. This hæmolytic effect, as well as its antibacterial effect, is very strongly reduced by serum albumin, and it is clear that biological activity can be related to the head-and-tail effect of the long branched-chain and the hydrophilic groupings. It appeared possible that by preserving the branched-chain fatty character of the substance while varying the hydrophilic groups, high biological activity might be preserved while reducing the binding effect of serum. This possibility has been realized by the replacement of the COOH and COOEt groups of (II) by $-CH_2OH$ and $-CH_2NR_2$.

The first modification was effected by the reduction of (I) by lithium aluminium hydride[2]. This afforded the butane diol

$$C_{12}H_{25}—CH(CH_2OH)—CH(CH_3)—CH_2OH$$
III

which showed an inhibitory dilution against *Myco. tuberculosis* of 50,000, reduced by serum to 10,000. Other butane diols similarly prepared from *mono-* and *di*-alkyl succinic acids showed no higher activity.

Table 1. Anti-tubercular activity of butan-1, 4-diols *in vitro*

$$R'—CH(R'')—CH_2OH$$

Diol	No.	Inhibitory dilution (broth)	Inhibitory dilution (serum broth)
$R' = C_9H_{19}$, $R'' = H$	370	50,000 100,000*	20,000 30,000*
$R' = C_{12}H_{25}$, $R' = CH_3$	355	50,000 100,000*	10,000 50,000*
$R' = C_{12}H_{25}$, $R'' = C_2H_5$	389	5,000 150,000*	5,000 15,000*
$R' = C_{14}H_{29}$, $R'' = H$	373	5,000 30,000*	10,000 50,000*

* Dilution allowing full growth as in control. Strain of tubercle bacillus employed: *H* 37*Rv*.

At this stage, a number of propane-diols was synthesized by reduction of the readily accessible alkyl malonic esters by the same reagent:

$$R—CH=(COOEt)_2 \rightarrow R—CH=(CH_2OH)_2$$
$$(R = C_9H_{17} \text{ to } C_{14}H_{29})$$
IV

The best of these was 2-hydroxymethyl-*n*-decan-1-ol ($(R = C_9H_{17})$; inhibitory dilution = 30,000; inhibitory dilution (serum) = 20,000)).

A pentane-diol, 4-hydroxymethyl-*n*-tetradecan-1-ol (V, for synthesis, see later) showed somewhat higher activity but was strongly antagonized by serum.

$$C_{10}H_{21}—CH(CH_2OH)—(CH_2)_2—CH_2OH$$
(inhibitory dilution = 75,000; inhibitory dilution (serum) = 10,000)
V

Before attempting further modification of the *B*.53 molecule, it seemed worth while to aim at producing, by further syntheses, branched-chain molecules incorporating an amino-group. The simplest compounds of this type were obtained by lithium aluminium hydride reduction of alkyl cyanoacetic esters:

$$R—CH(CN)—COOEt \rightarrow R—CH(CH_2OH)—CH_2NH_2$$
$$(R = C_{10}H_{21} \text{ to } C_{14}H_{29})$$
VI

These simple amino-alcohols are very much more active than the corresponding diols, and serum antagonism is weak. Thus the compound, 406, 2-hydroxymethyl-*n*-dodecan-1-amine, has inhibitory dilution = 200,000 and only allows full growth at 500,000. Serum reduces these figures to 75,000 and 100,000 respectively. A comparison of these figures (Table 2) with the activities of the corresponding propanediol showed that we were moving in the right direction.

Table 2. Anti-tubercular activity of hydroxy-amines VI *in vitro*

$$R\,CH(CH_2OH)—CH_2NH_2$$

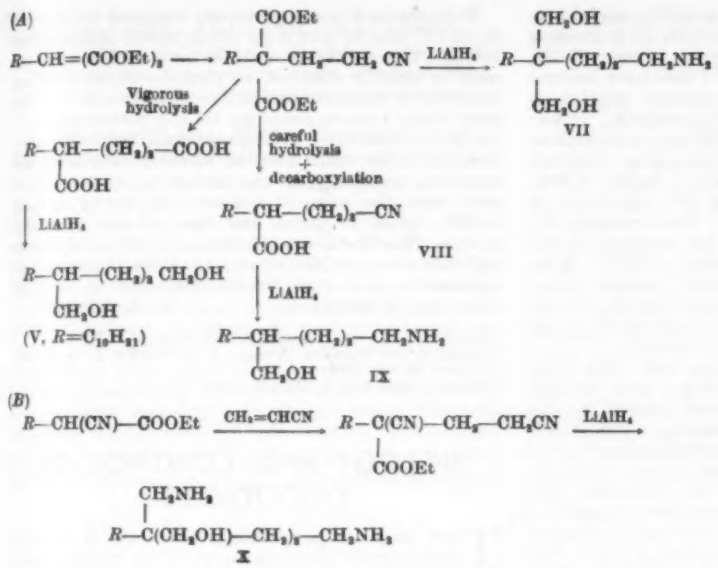
(VI)	No.	Inhibition dilution (broth)	Inhibition dilution (serum broth)
$R = C_{10}H_{21}$	406	200,000 500,000*	75,000 100,000*
$R = C_{12}H_{25}$	372	75,000 300,000*	50,000 75,000*
$R = C_{14}H_{29}$	387	30,000 500,000*	20,000 50,000*

* Dilution allowing full growth as in control. Strain of tubercle bacillus employed: *H* 37*Rv*.

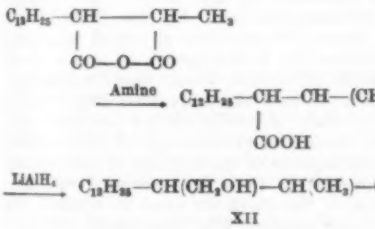
Related compounds containing primary amino- and alcohol groupings were obtained by condensing alkyl malonic esters and alkyl cyanoacetic esters with acrylonitrile (4) and then proceeding according to the schemes *A* and *B* outlined.

(VII, $R = C_{12}H_{25}$), that is, 4-*bis*hydroxymethyl-*n*-hexadecan-1-amine, has an inhibitory dilution of 100,000, reduced by serum to 20,000, whereas (IX, $R = C_{12}H_{25}$), with one primary alcohol group replaced by hydrogen, has a much greater activity (inhibitory dilution = 300,000; inhibitory dilution (serum) = 100,000). The extra amino-group in (X) again proves not to be advantageous. Thus when $R = C_{10}H_{21}$, (X) has inhibitory dilution = 200,000 and inhibitory dilution (serum) = 75,000. In passing, it is worth noting that the cyano-acids (VIII) are much less active. The compound (VIII, $R = C_{12}H_{25}$) inhibits completely at a dilution of 75,000 and at 10,000 in the presence of serum.

The branched-chain hydroxy-amines (IX) were obviously of great promise, and it became of interest



to determine whether a similar type of compound with the specific *B.*53 hydrocarbon skeleton would prove to have greater antitubercular activity *in vitro*. Synthesis of primary, secondary and tertiary branched-chain amines containing a $-CH_2OH$ group was attempted according to the following method:



The compound (XI) obtained when ammonia was employed, 2-methyl-3-hydroxymethyl-*n*-pentadecan-1-amine, has not been obtained pure, but exhibits, nevertheless, a considerable antitubercular potency*. It completely inhibits *Myco. tuberculosis* at a dilution of 200,000 and does not permit full growth until a dilution of 2×10^6 is reached. Analytically pure oils were obtained when the ammonia was replaced by methyl-aniline and diethylamine. (XII, $R' = CH_3$; $R'' = Ph$) shows low activity (inhibitory dilution = 10,000; inhibitory dilution (serum) = 10,000). On the other hand, (XII, $R' = R'' = C_2H_5$) is very active, producing complete inhibition in broth at a dilution of 500,000 and partial inhibition up to 1×10^6. These figures are only reduced by serum to 100,000 and 200,000 respectively. We have therefore succeeded in a planned modification of the *B.*53 molecule which has resulted in a compound which exhibits a somewhat higher anti-tubercular activity in broth than *B.*53 and has ten times the activity in serum broth.

Further synthetical possibilities in this field are being explored. When a sufficient quantity of (XII, $R' = R'' = Et$) has been accumulated, it will be submitted to a trial in guinea pig tuberculosis.

Our thanks are due to our colleagues, Dr. M. L. Conalty and J. F. Chambers, who conducted the *in vitro* tests on these compounds, and to Mr. T. J. D. Lane, for a preliminary account of his clinical experience with *B.*53 in vesical tuberculosis. Grateful acknowledgment is also made to Mr. Max Gergel, Columbia Organic Chemicals Co., for the gift of chemicals.

* *Note added in proof.* We have since obtained evidence that where ammonia or a primary amine is employed in the preparation of the half-amide, subsequent $LiAlH_4$ reduction leads to the formation to some extent of pyrollidine derivatives. Ring closure appears to have occurred also in the synthesis of (X).

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NEW SIMPLIFIED ELECTRON MICROSCOPES

ELECTRON microscopes, of both electrostatic and magnetic type, are now manufactured commercially in several countries. Most of the models on the market have a resolving power in the range 50–100 A., although in the hands of specialists selected instruments have been shown capable of a resolution better than 20 A. However, such tuning-up demands considerable time and experimental skill, and at the same time it is found that most of the applications of the instrument, whether in biology or metallurgy, at present call for a resolution no better than 100 A. Hence there is no great pressure on the designers to produce machines to more stringent specification. Indeed, a survey carried out by the Radio Corporation of America[1] showed that there was an appreciable demand for a machine to cover the range from the normal limits of optical microscopy (about 2,000 A.) to a resolution better by an order of magnitude only. Such an electron microscope could be made simpler and more compact, and thus would be at the same time easier to operate and maintain, and cheaper, than the standard models.

Acting on this consumer survey, the Radio Corporation of America produced a "console model" (Type *EMC*), which is described by Zworykin and Hillier[1]. It proved in practice to be too limited in performance to meet practical needs: the accelerating voltage was low (30 kV.) and the illumination weak, so that only very thin specimens could be observed, and at moderate magnification (5,000). It has therefore had only a restricted use, in spite of attempts to improve it.

Evidence of the need for such a utility model has, however, continued to accumulate with the increasing application of the electron microscope in many fields, and particularly since a number of uses have become sufficiently standardized as to become routine in nature, for example, in particle-size analysis. It was not surprising, therefore, that Metropolitan-Vickers should have followed its recent three-stage standard model (*EM*3) by designing a cabinet model (*EM*4), which was shown last March at the exhibition in London of the Physical Society. More recently the Radio Corporation of America has announced the appearance of a new table model (*EMT*). Both machines have a number of novel features, apart from the general simplification and reduction of cost which place them in a separate category from all other electron microscopes so far produced.

The *EM*4 is designed as a single unit, with high-tension generator, smoothing circuits and vacuum pumps all contained in the same cabinet as the microscope proper and its controls. The *EMT* consists of four separate units, allowing the microscope itself to be separately mounted along with the diffusion pump and some of the controls. The length of the column is kept to reasonable size (30 in.) by dispensing with a condenser lens and employing a moderate magnification (maximum, 6,000). The *EM*4 achieves a column of about half this length, with a wide range of magnification (up to a maximum of 20,000), by using a projector lens having three magnetic gaps in place of the usual single gap. It thus acts as a four-stage microscope, instead of two-stage; the length of column is proportional to the sum of the separate magnifications, while the maximum magnification is given by their product. The resulting short column is fixed horizontally in the top of the cabinet, with the camera chamber at the front end. For visual observation, a magnetic deflecting field throws the image on to an inclined window above the camera. This innovation allows ready observation in a sitting position and simplicity of camera operation; the camera takes either roll film or plates. On the electrical side the *EM*4 incorporates dry rectifiers and voltage doubling in the high-tension supply, in order again to achieve compactness and reduction in cost, as compared with the conventional transformer – rectifying-valve system. In other respects the new model is a simplified version of the *EM*3 instrument, apart from the inclusion of a beam-vibrator for ease of focusing.

The chief technical interest in the new American model, apart from the general design and mounting of the column, lies in the use of permanent magnets instead of energized windings for the objective and projector lenses. A machine of standard type was made some years ago using permanent magnets[2], and von Borries recently described a simpler arrangement[3]; but no commercial model has previously departed from the use of coils for the magnetic lenses. In the Radio Corporation of America design the microscope column is near-vertical, with camera and viewing-window at the bottom end. The magnetic circuit has two gaps, the upper forming the objective and the lower the projector lens. The magnification is fixed, there being no means of varying the reluctance of the circuit. Lens units giving magnifications of 1,500, 3,000 and 6,000 are available. As the positions of both lens and object are fixed, focusing is carried out by varying the accelerating voltage applied to the anode.

Both the new instruments are designed to operate at 50 kV. and to give a resolving power approaching 100 A. The specimen and the photographic plates may be quickly changed, so that the rapid working desirable in routine applications is achieved. If the production models come up to the performance of the prototypes, they will represent an important step towards wider utilization of electron microscopical methods, especially at the technological level. In each case the price is indicated as being around £2,000, which is about half that of the standard models. The specified performance is certainly above half that shown by the latter; the *EM*4, in particular, appears to have considerable flexibility as well as simplicity of operation. V. E. COSSLETT

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BIOLOGY AND CONTROL OF COCCIDIOSIS

THE range of parasitology nowadays is so wide that anyone choosing to work on it soon finds that he must not only have a very broad scientific training, but must also restrict his studies to one field, or even to one genus of parasitic animals. If he be interested in the Protozoa, for example, he may well find that the study of coccidiosis, or even the study of the economic aspects of this disease, will occupy all his life.

For anyone interested in this subject, the conference on coccidiosis convened by the New York Academy of Sciences* provides a sound synoptic view of it. Prefaced by a photograph of, and a short article by, Prof. E. E. Tyzzer, whose classic researches on the coccidia of hen chickens and other birds established the study of coccidiosis for the first time on a scientific basis, the proceedings of this conference cover most aspects of the biology of the species of coccidia considered, their host-parasite relationships and most of the methods used to control the diseases that they cause. The importance of their control is shown by the estimate worked out by one contributor that coccidiosis of poultry costs the United States ten million dollars a year, coccidiosis of cattle the same figure and coccidiosis of sheep half a million dollars, while the disease in goats, pigs, dogs, cats, rabbits and fur bearers adds another half-million dollars to the cost. The total cost of the disease in the United States is thus twenty-one million dollars a year.

It is impossible to summarize in a short space the wide range of this conference. It provides a valuable epitome of every aspect of the subject, and articles on the chemotherapy of the disease and on its nutritional aspects illustrate well the degree to which the parasitologist nowadays has to be, or has to try to be, a biochemist. Although most of the work is American, British research is represented by the article, contributed by Dr. C. Horton-Smith, on factors which influence the origin and course of epidemics of coccidiosis in poultry. The bibliographies appended to each article are a valuable feature of the publication.

* *Annals of the New York Academy of Sciences*, **52**, Art. 4: Coccidiosis. By S. Blackett and forty-two other Authors. Pp. 429–624. (New York: New York Academy of Sciences, 1949.) 3 dollars.

LETTERS TO THE EDITORS

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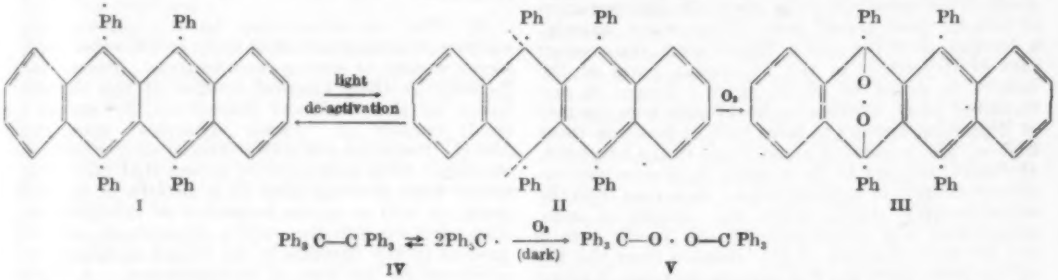
Demonstrability of the Photochemical Formation of Biradicals by Magnetic Methods

THE red 5,6,11,12-tetraphenylnaphthacene (rubrene) (I) is stable to oxygen in the solid state; its solutions, however, are only stable in the dark. When they are irradiated with sunlight or artificial light in the presence of oxygen, a crystalline peroxide (III) is formed[1] (the quantum efficiency of the formation of (III)[2] rises to unity at concentrations greater than 0·01 molar and is independent of wave-length between 3660 and 5460 A.). The easy formation of this peroxide is reminiscent of the formation of (V) from solutions containing hexaphenylethane molecules, as well as their dissociation products, namely, the paramagnetic triphenylmethyl radicals (IV). (The schemes II $\xrightarrow{O_2}$ III and IV $\xrightarrow{O_2}$ V are simplified ones and show in both cases only the initial and final products.)



$$Ph_3C{-}CPh_3 \rightleftarrows 2Ph_3C\cdot \xrightarrow[(dark)]{O_2} Ph_3C{-}O\cdot O{-}CPh_3$$

IV V

It has been assumed[3] that light energy transforms the ordinary form of rubrene (I) into a biradical (II), an analogue of triphenylmethyl; it is believed that (II), which should be paramagnetic according to this hypothesis, is able to return to the non-activated diamagnetic state by re-arrangement of the electrons (II → I).

It has been repeatedly stated that the hypothesis of the photoformation of (II) has not been confirmed or has even been contradicted[4] by magnetic measurements, and the criticism is based on Müller's work[5]. According to him, irradiated and non-irradiated solutions of rubrene do not differ in their magnetic properties. No details have been published concerning the photo-experiments, for example, the intensity and nature of the light used in the experiment.

Müller's experiments can, however, scarcely be accepted as evidence against the formation of (III) via a biradical mechanism (comp. II), as the following calculations show that it is very difficult to detect the photochemical formation of activated paramagnetic molecules, in consequence of their low concentration, by the method applied by Müller.

Let q denote the rate of the photo-activation process I → II, x the number of activated molecules (radicals) II present at a given time, both q and x expressed as fractions of the total number of molecules (I). Denote by τ the life-time of a radical (II) before returning to (I); then $1/\tau$ is the probability of deactivation II → I per unit time. One has for the reaction velocity the equation

$$\frac{dx}{dt} = -\frac{x}{\tau} + q,$$

the solution of which satisfying the initial condition $x(0) = 0$ is

$$x = q\tau\{1 - \exp(-t/\tau)\}.$$

It tends to the stationary state $x = q\tau$.

One can estimate that with the sources available for these experiments (300-watt lamp) the number of photons absorbed is about 10^9 per second per mole; hence, as only part of these photons are used for activation, one has $q < 10^{-4}$ sec.$^{-1}$. Hence $\tau > 10^4 x$ sec.

The sensitivity for discovering magnetic radicals ought to be, therefore, better than $x \sim 10^{-4}$ in order to have the lower limit of τ of the order of 1 sec. It is not very likely that life-times of diradicals produced by photo-activation are so long. With the Curie balance the limit of detection is about 1 per cent, $x = 10^{-2}$, hence $\tau > 100$ sec. A life-time of this length would be observable by the retardation of the establishment of equilibrium. In fact, no such time-lag has been observed.

The extremely low concentration of the photo-activated molecules is not inconsistent with the fact that (III) is formed rather rapidly; activated molecules which disappear from the photo-equilibrium (I ⇌ II) in consequence of de-activation or peroxide formation are replaced almost instantaneously; the disadvantage of the low concentration of the activated molecules is counterbalanced by their rapid reformation.

It is hoped that, by the application of a more sensitive method (magnetic resonance may be tried) such as the one used by Müller, the question whether photo-activated organic molecules may be paramagnetic in spite of the fact that the non-activated form is diamagnetic will be solved. This question is also important in connexion with the problem of photo-sensitization[6].

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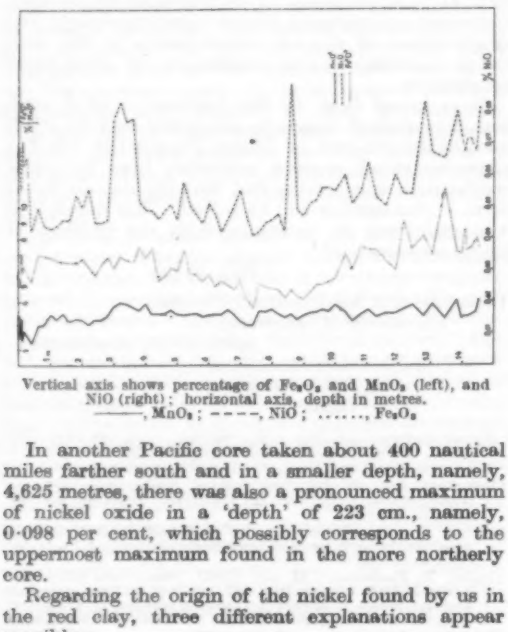
Nickel Content of Deep-Sea Deposits

INVESTIGATIONS made in this Institute of the ferrides present in sediment cores from great depths, taken by the Swedish Deep-Sea Expedition, have shown their content of nickel to be specially interesting. The only analysis of nickel in deep-sea deposits known to us was published in 1914 by F. W. Clarke and G. Steiger, and gave 0·032 per cent as the content of nickel oxide in a composite sample of red clay from fifty-one different localities[1]. By the aid of modern microanalytical methods (the colour reaction with dimethyl glyoxime) quantities of nickel as small as 5–6 γ can easily be measured.

In a core of red clay from the north-west Atlantic Ocean (lat. 30° 29′ N., long. 56° 07′ W., depth 5,620 metres, length of core 1,530 cm.) the content of nickel oxide was found to vary between 0·005 and 0·010 per cent, whereas in a red clay core from the central Pacific Ocean (lat. 07° 38′ S., long. 152° 53′ W., depth 5,000 metres, length of core 1,500 cm.) much higher values were found, ranging between 0·041 and 0·089 per cent of nickel oxide. Assuming the decrease in radium content from the surface layer downwards found in the latter core to be due to the disintegration of ionium, precipitated from the sea-water, namely, a decrease to 50 per cent in 83,000 years, the average rate of deposition in the uppermost parts of the same core would be of the order 0·5 mm. in one thousand years, whereas in the Atlantic core the rate of deposition appears to have been at least ten times higher. The content of nickel oxide in the two cores, therefore, appears to be roughly in inverse proportion to the rate of sedimentation. As is seen from the accompanying graph, where the content of iron-, manganese- and nickel-oxide in the Pacific core is set out as a function of the distance from the top of the core, there are five distinct maxima of nickel content, which do not seem to be related to those of the two other elements.



Vertical axis shows percentage of Fe_2O_3 and MnO_2 (left), and NiO (right); horizontal axis, depth in metres.
———, MnO_2; – – – –, NiO; ....., Fe_2O_3

In another Pacific core taken about 400 nautical miles farther south and in a smaller depth, namely, 4,625 metres, there was also a pronounced maximum of nickel oxide in a 'depth' of 223 cm., namely, 0·098 per cent, which possibly corresponds to the uppermost maximum found in the more northerly core.

Regarding the origin of the nickel found by us in the red clay, three different explanations appear possible:

(1) It may have originated from sea water. This, however, appears improbable, considering the extremely low nickel content in the water (about 10^{-6} per cent or about 500 times less than its content of iron).

(2) It may have originated from magma spread over the ocean floor by submarine eruptions. Thanks to the courtesy of Dr. S. Landergren of the Geological Survey in Stockholm, we have had various specimens of submarine and supramarine lava from the central Pacific Ocean, as well as basaltic rock fragments, taken from great depths in the Indian Ocean by the John Murray Expedition, analysed for nickel by spectrographic precision methods. The results were low, varying between 0·005 and 0·012 per cent. Further, a layer rich in volcanic minerals taken immediately below the layer of maximum nickel content just mentioned was found to have values similar to those of average samples taken from the same core. A magmatic origin of the high nickel values we have found, although it cannot at present be ruled out, appears, therefore, not very probable.

(3) That the nickel may have originated from meteors and from meteoritic dust, on the other hand, seems worthy of serious consideration. Murray and Renard, in their classical studies of the deposits taken by the *Challenger* Expedition, recognized a small number of "cosmic spherules" containing nickel–iron in the red clay and other similar deep-sea deposits. It is reasonable to expect that other fragments from shooting stars in a metallic or oxidized state, as well as minor fragments of interplanetary dust, drifting into the earth's atmosphere, must be present in the deposits to an extent inversely proportional to the rate of sedimentation. A highly approximate calculation, from what we know at present regarding the nickel content and the rate of sedimentation of the cores we have so far examined, leads to unexpectedly high values for the rate of accretion of meteoric material over the whole earth. Our estimates indicate several thousand tons per day (assuming an average nickel content of 2 per cent by weight), which is considerably more than astronomers are at present prepared to admit, on the basis of visual and telescopic counts of meteors entering the earth's atmosphere.

Should a cosmic origin of at least the greater part of the nickel found in the red clay be accepted as a working hypothesis, special interest is attached to the maxima shown by the curve. They might be explained as indicating occurrences of an increased frequency of meteors in the past, possibly due to the solar system travelling through relatively dense cosmic clouds, affording increased chances of capturing comets and meteors.

Investigations now being undertaken will have to show whether such maxima of nickel content coincide with maxima in the number of cosmic spherules, and whether they are of world-wide occurrence. Anyhow, it appears desirable to submit future deep-sea cores to a systematic search for nickel.

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Titrimetric Determination of Nitrates with an Equivalent Ratio of 1 : 8

MANY procedures for titrimetric nitrate determinations are based on reduction by ferrous salts. Ferrous iron reduces nitrates boiled in acid medium to nitrous oxide. In alkaline medium the reduction proceeds at a concentration of 28 per cent sodium hydroxide, and the product is ammonia. Cotte and Kahane[1] have found that silver sulphate catalyses the reduction at a suitably lower concentration of hydroxide. The ammonia formed was distilled into acid, the excess of which was measured. Our method is based on the same reduction; but the reduced nitrate is measured in another manner. The reduction is effected in a boiling 3 per cent sodium hydroxide solution, containing ammoniacal silver sulphate, by the action of ferrous hydroxide precipitated from a measured sample of ferrous ammonium sulphate. When the reaction is completed, the mixture is acidified with sulphuric acid and the excess of the ferrous iron is titrated with potassium permanganate. A blank titration must also be carried out. The reduction—without regard to the catalysis—proceeds by the following reactions:

(1) $KNO_3 + 2\ Fe(OH)_2 + H_2O = KNO_2 + 2\ Fe(OH)_3$;

(2) $KNO_3 + 6\ Fe(OH)_2 + 5\ H_2O = 6\ Fe(OH)_3 + NH_3 + KOH$.

As can be seen from the equations, 8 moles of $Fe(OH)_2$ are necessary for the reduction of 1 mole of nitrate. 1 ml. of 0·1 *N* potassium permanganate is equivalent to 0·7751 mgm. of NO_3.

Blank: 45·96 ml. 0·1 *N* potassium permanganate

Nitrate taken (mgm.)	0·1 *N* permanganate (ml.)	Nitrate found (mgm.)	(%)	Difference (mgm.)
1·882	43·48	1·922	102·14	+0·040
4·662	39·93	4·674	100·26	+0·012
9·335	33·94	9·317	99·81	−0·018
13·998	27·94	13·967	99·78	−0·031
18·652	21·94	18·618	99·82	−0·034

The largest quantity of nitrate which it was possible to determine amounted to 20 mgm., assuming the use of a 50-ml. burette. This is only equivalent to about 26 ml. of permanganate; but the ferrous ammonium sulphate must be employed for the reduction in large excess owing to the formation of ferrous – ferric oxide. The fact that the errors of the different nitrate concentrations are quite constant indicates the introduction of correction values.

The ions Al^{3+}, Zn^{2+}, Cd^{2+}, As^{5+}, Sn^{4+}, Mo^{6+}, U^{6+}, W^{6+}, Cl^-, PO_4^{3-}, $B_4O_7^{2-}$, CH_3COO^-, ClO_4^- do not interfere with the method. The interference of the ions: V, As^{3+}, Sn^{2+}, Co^{2+}, Ni^{2+}, Mn^{2+}, Br^-, ClO_3^-, CO_3^{--}, HCO_3^-, $S_2O_3^{2-}$ can be easily eliminated or compensated.

A detailed communication on this subject will be published in the *Hungarica Chimica Acta*.

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Production of Staphylocoagulase in a Chemically Defined Medium

IN the course of work on the purification of staphylocoagulase, a possible approach appeared to be the production of the enzyme in a protein-free 'synthetic' medium. While growth of *Staphylococcus aureus* occurs according to Fildes *et al.*[1], Gladstone[2] and Gale[3] in media simpler than that reported here, for our purpose, which is concerned exclusively with the production of coagulase, a medium containing a wide range of amino-acids and vitamins seemed advisable. This medium has yielded good growth of a number of freshly isolated strains of coagulase-positive staphylococci, without prior 'training'.

The composition of the medium per hundred c.c. of fluid is as follows: 0·025 gm. each of L-cystine, L-histidine, L-leucine, L-phenylalanine, L-proline, L-tryptophane and L-tyrosine; 0·05 gm. each of L-arginine, glycine, DL-*iso*leucine, L-lysine, DL-methionine, DL-serine, DL-threonine and DL-valine; 0·125 gm. of both DL-aspartic acid and L-glutamic acid; 0·05 µgm. of biotin; 0·125 gm. each of $MgSO_4.7H_2O$, dipotassium hydrogen phosphate, sodium chloride and ferrous sulphate (crys.); nicotinamide, pyridoxine and thiamine each at a concentration of 0·0005 *M*. All constituents were dissolved separately as stock solutions: the amino-acids with the exception of cystine and tyrosine in Sörensen's buffer *p*H 7·3; cystine and tyrosine in 3 *N* hydrochloric acid afterwards diluted with distilled water; salts and vitamins in distilled water. All solutions were sterilized by autoclaving except the ferrous sulphate, which was always freshly prepared and sterilized by filtration through a Seitz pad. The medium, made up by mixing the stock solutions, had a final *p*H of 7. 10 c.c. amounts were distributed with aseptic precautions into universal containers.

The original inoculum consisted of a saline suspension of cells, obtained by repeated spinning and washing of a 24-hours broth culture; serial subcultures were then obtained by transferring one loopful of growth in synthetic medium. Cultures were incubated at 37° C., samples withdrawn every twenty-four hours and sterilized by heating at 65° C. for 45 min. To 0·5 c.c. of such a killed culture or to a dilution of it, 0·1 c.c. of heparin (containing 10 international units) and 0·2 c.c. of human citrated plasma were added. The mixtures were incubated for twenty-four hours and the sterility of the clots tested by adding 4 c.c. of broth and incubating further.

Coagulase was demonstrated both in the primary cultures and in all sub-cultures. The amount of coagulase was small—not exceeding a titre of 1 : 16; this was generally reached after three to five days incubation of the cultures. It has been recently reported[4], however, that purified coagulase shows increased thermolability, and results obtained by one of us (A. J. O'H.) appear to support this. The evidence points to coagulase being present in the medium in a state of relatively high purity and, therefore, heat-sensitive. Thus, the titre of the enzyme demonstrated probably represents only a fraction of that actually produced in the medium. Despite the low titres so far attained, the preparation of staphylocoagulase in a protein-free medium of known chemical composition was thought interesting by itself as an instance of production of a bacterial enzyme under controllable conditions.

We are indebted to the Rankin Research Fund for a grant towards the expenses of the work. We

also wish to thank British Drug Houses, Ltd., Roche Products, Ltd., and British Chemicals and Biologicals, Ltd., for valuable information regarding the amino-acids which they have supplied.

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A Cephalinase in Nervous Tissue

The phospholipids were regarded by the older investigators as relatively inert, and for this reason they have been classed among the 'permanent' or structural elements of the cell. Experiments with the radioactive isotope, phosphorus-32, have shown, however, that the phospholipids of the brain have a significant phosphorus turnover-rate[1,2], and the turnover is greater for cephalin than lecithin.

When sterile rat brain tissue, or a homogenate containing buffer (pH 7·5), is incubated at 37° C. in the presence of 1/2,000 merthiolate to prevent bacterial growth, there is a fall in the phospholipid content. Thus in eight experiments the mean phospholipid content of the whole rat brain fell from 4·92 per cent tissue weight to 4·30 per cent in twenty-four hours at 37° C. Determination of the different phospholipid fractions, by methods similar to those described by Hack[3], showed no significant change in the sphingomyelins: the lecithin content fell only from 1·44 to 1·29 per cent, and the main change was in the cephalin fraction, which showed a significant fall from 2·84 to 2·40 per cent.

The decomposition of cephalin is apparently due to an enzyme which splits off the phosphate-containing residue; this is then further broken down by phosphatase action to liberate inorganic phosphate, which could be shown to be formed. The cephalinase has relatively little or no action on lecithin in brain homogenates; for this reason it apparently differs from the lecithinase previously described by King[4].

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Effects of 'Aminopterin' on the Male Sex Organs of the Guinea Pig

Following the interesting communication by Hertz[1] on the decreased growth response of the oviduct to œstrogens in chicks fed on a purified diet without folic acid intake, many reports have appeared lately showing that, in the animals studied, either folic-acid deficiency[2,3] or treatment with 'Aminopterin'[4-7] were able to interfere with the growth response to œstrogens of the female genital tract.

On the basis of these experiments and because of the fact that 'Aminopterin' has been shown to interfere with the ordinary depressive influence of œstrogens on the rat prostate[8], it has been reasonably assumed that folic acid is a prerequisite for the proper utilization of œstrogens. Whether folic acid might also be a prerequisite for the proper utilization of androgens has also been studied; but the results have been discordant. Breudler[9] reported that 'Aminopterin' did not interfere with androgen stimulation of tissue growth in castrated adult and immature rats. On the other hand, Goldsmith and others[8] reported that, in mice fed a crude folic acid antagonist, a reduced response to androgen was evident in the vesicular and coagulating glands.

In the following experiments the effects of 'Aminopterin' on the sex organs of the intact adult guinea pig are studied. The guinea pig was chosen because this animal has no rutting season. Twenty guinea pigs (median weight 600 gm.) were divided into two groups of ten each. Each animal of the first group received 1 mgm. of 'Aminopterin' (kindly supplied by Dr. J. M. Ruegsegger, of the Lederle Laboratories Division of the American Cyanamid Co., Pearl River, New York) intraperitoneally every day for eight days. The animals of the second group received the same amount of 'Aminopterin' for fifteen days.

All the animals in the first group were killed on the eighth day, and the testicles, epididymis, prostate and vesicular glands were studied comparatively with the same organs belonging to five guinea pigs of the same weight used as controls. Grossly, the epididymis, the testicle and the prostate of the guinea pigs receiving 'Aminopterin' did not show any appreciable damage. The vesicular glands, on the other hand, did show an evident decreased size in comparison with the controls. The histological study of the material revealed no apparent change in the testicle; the tubules of the epididymis of some of the animals were almost devoid of spermatozoa, while the epididymis of the controls was overloaded with spermatozoa. In the vesicular glands of the treated animals, the natural infolding of the mucosa was clearly less accentuated than in the controls. Slight signs of atrophy were present in the prostate.

In the second group, although the 'Aminopterin' was given for a period twice as long, the same findings were noticed as in the first group. Hence it may be assumed that the effects of 'Aminopterin' on the male sex organs are not striking if we consider the high doses of the drug being used. In any event, the most evident changes are on the epididymis, which contains less spermatozoa, and on the vesicular glands, which are clearly reduced in size.

I am grateful to Dr. John Mackrell for examining the histological material.

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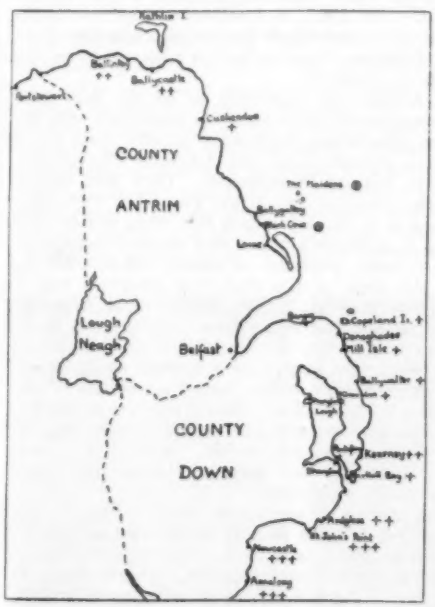
Distribution of *Chthamalus stellatus* on the Shores of North-East Ireland

In a paper discussing the distribution of *Chthamalus stellatus* in British waters, H. B. Moore and J. A. Kitching[1] attempted to link up the distribution of this barnacle with that of Atlantic water. Recently, Kitching[2] suggests that air temperature may be the limiting factor, abandoning to some extent the Atlantic water theory, but adding "although from the known facts the latter is equally possible". Southward[3] has recently recorded the general occurrence of *Chthamalus* in the Isle of Man, and he too points out that there appears to be some correlation between air temperature and the distribution of the species. In the map of Moore and Kitching, *Chthamalus* is unrecorded between Howth and Belfast Lough and given as absent from the east coast of Antrim but as present at Portstewart on the north coast. It was also recorded as absent from the Isle of Man.

Since 1938 I have known of the occurrence of *Chthamalus* in County Down, and it was later recorded by MacDonald[4] from Portlehan near Ardglass. Within the past three months, I have obtained specimens from the following places in Down: Annalong, Newcastle, St. John's Point, very abundant; Ardglass and Kearney, abundant; Bar Hall Bay and Kircubbin (in Strangford Lough), less numerous; Ballywalter, Mill Isle and the Copeland Islands, rather scarce. Although a careful search was made, I have been unable to find *Chthamalus* on the coast of Down north of Mill Isle; but much of this part of the coast is unsuitable for such a high water mark species. A recent examination of County Antrim shows that *Chthamalus* is abundant at Ballintoy and Ballycastle on the north coast, less abundant at Cushendun and present in very small numbers at Black Cove between Larne and Ballygalley. It also occurs on both the larger islands of the Maiden group, but is not at all abundant.



Coastline of Counties Down and Antrim to show the relative abundance of *Chthamalus stellatus*

+++ = very abundant. ++ = abundant. + = present, but not abundant. ⊕ = present, but very scarce

At all the localities where I have found *Chthamalus stellatus* to be abundant, it is commonly found on fairly exposed surfaces above the *Balanus* zone; but at the Copeland Islands, Ballywalter and Mill Isle in northern Down and at Black Cove in Antrim and at the Maidens, it is encountered mixed with the *Balanus* population and is not distinctly above this zone. Furthermore, in these localities it seems to favour the corner of a small crevice or the flat surface of a deep narrow fissure the width of which is just sufficient to allow the barnacle to grow. Such relatively protected sites are commonly found, however, in the narrow upper ends of gullies subject to good wave action. In the Ballycastle and Ballintoy localities it is again abundant on exposed surfaces in the splash zone above the *Balanus* zone.

My observations do not support the theory that it is Atlantic water which favourably influences the distribution of *Chthamalus*, for the colonies at Newcastle, Annalong, Ardglass and Kearney, where *Chthamalus* is abundant, are much less subject to the influence of Atlantic water than are those at Cushendun, Black Cove and the Maidens, yet it can be found in the last two localities only after diligent search. Since the east coast of Antrim is subject to a lower winter air temperature than the coast of Down, it seems more probable that the air temperature is the chief factor controlling the distribution of *Chthamalus*. Moreover, a fluctuating distribution is much more indicative of a variable limiting factor such as air temperature than the degree of Atlantic water, which presumably is approximately the same each year.

I am glad to acknowledge discussions of the question with Prof. R. A. R. Gresson and Mr. R. V. Gotto.

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Breeding and Distribution of *Chthamalus stellatus*

Recent suggestions have been made relating the distribution of *Chthamalus stellatus*[1,2] to low-temperature isotherms. It may therefore be of value to put on record some new observations on its breeding made over the past three years, which have a bearing on present distribution.

Chthamalus is much more widespread in the Irish Sea than is suggested either by Moore and Kitching[1] or by Southward[3]. It has been found to be present along the whole Ayrshire, Galloway, Cumberland and Lancashire coasts as far south as New Brighton (1950). The settlement, even at Blackpool, is not a casual one but contains individuals of large and small sizes (0·2–1·4 cm.) representing probably at least three years settlements. It reappears just south of Holyhead at Porth Dafarch in considerable numbers. The main area of absence on the English coast is thus sharply defined, and limited to the north coast of Wales and Anglesey. Whether this present distribution is the result of two recent warm summers (1947 and 1949) followed by mild winters (since

1946–47), together with a period of rather low average rainfall, or whether the distribution contours of Moore and Kitching were inaccurate for this area can only be decided by subsequent observations, as Moore and Kitching made no direct records between Millport (present) and Leasowe embankment (absent). Their distribution line was determined by reported absences from the Mull of Kintyre and Co. Antrim, an area where conditions, apart from small intertidal range, would all appear favourable; certainly more favourable than on the sandy coast of the Fylde with only few artificial substrata present. Chipperfield[3] has recently re-examined a collection of cirripedes from the upper barnacle zone at Port Erin and Port St. Mary (Isle of Man) taken in 1946, and found the whole of the seven hundred individuals were *Balanus balanoides*. *Chthamalus* would appear, therefore, to have been either absent, quite rare or very local at this time. On the other hand, Mr. H. Powell[4] kindly compared with the present population photographs taken at Farland Point (Cumbrae) in 1946, on which *Chthamali* were clearly visible, and considered that there had been no apparent increase to date, although the general density was actually less than that reported by Moore and Kitching. No significant difference in the position of the limits has been observed either on Anglesey or in the Dorset area during a recent re-examination (1949–50), limits which might be equally liable to variation on account of climatic fluctuations.

Chthamalus starts to breed considerably earlier than previously reported[5], although the occurrence of nauplii during January–March[6] is surely due to confusion with *Balanus balanoides*. In the south-west (Brixham–Penzance) fertilized eggs are to be found in occasional individuals at low-water mark by the first week in April, the onset of fertilization gradually spreading up the intertidal zone, reaching the level of high-water springs by late May. Farther north, fertilization commences only a little later, Westward Ho! (North Devon) in mid-April, North Wales and the Fylde in late April, and Cumbrae (Scotland) in early May. The date of fertilization is also a little later towards the east. Fertilization occurs right up to the limit of distribution wherever individuals are sufficiently close together. Individuals separated by a distance greater than that of the extended penis probably do not fertilize, as is the case in *Balanus balanoides*[7], *Elminius modestus* and *Balanus crenatus*. This feature, probably quite general in cirripedes, is very important in distribution, since fair settlements are necessary before a population can stabilize itself in a new situation. Thus, if environmental factors are marginal, as they may well be for *Chthamalus* in the Irish Sea, the boundary of distribution may fluctuate; but the population will at any one time cover a discrete and distinct area within which there are enough closely placed individuals to maintain the population.

Chthamalus, like *Balanus crenatus* and *Elminius* but unlike *Balanus balanoides* in British waters, gives rise to a succession of broods during its breeding season, the ovaries re-developing as each brood matures. Of these broods, which are liberated as nauplii from early May until late September, only those appearing in the plankton during July–August succeed in passing through the later larval stages and settling. Whatever unfavourable influence operates during the earlier and later months in the south-west may operate for an increasing proportion of the breeding period towards the distribution limits. The vulnerability of the larval, rather than adult, stages is emphasized by the survival of transplants in good condition over the winter of 1949–50 at Whitley Bay even at high-water springs level.

The better survival of *Chthamalus* at high water and in exposed situations with on-shore winds[7] is probably related to its feeding habit. In situations over which wave swash occurs, individuals may be observed feeding not by cirral beat, but by holding the cirri stiffly against the stream, retracting only occasionally (on capture of food?) or when the water drains off. The adults in such situations are not only more strongly growing but also produce nauplii earlier and at more frequent intervals than do those in sheltered positions.

I wish to thank Prof. J. H. Orton, Dr. P. N. J. Chipperfield and Dr. J. A. Kitching for stimulating discussions on this subject.

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The Medusa *Craspedacusta* in Australia

The Trachyline medusa *Craspedacusta sowerbii* Lankester (*Mycrohydra ryderi* Potts) has made several sporadic appearances in Great Britain and the continents of Europe and America since it was first described by Lankester[1] from specimens found in the *Victoria regia* tank in Regent's Park, London, in 1880. In 1907, a freshwater medusa under the name of *Limnocodium kawaii* Oka was described from the Yangtse; but this is now believed to be identical with *C. sowerbii*[2].

I believe the following to be the first record of the species on the Australian continent. On March 8 some specimens were very kindly sent to me by Mr. J. Johnston, of the Adelaide Engineering and Water Supply Department. They had been found on the previous day in the Thorndon Park reservoir, which is in the foothills a few miles out of Adelaide. This is Adelaide's oldest and smallest reservoir, having a total capacity of about 138,500,000 gallons. At the time of the find, the reservoir was nearly three-quarters full; in shape, it is more or less circular and has stone-faced revetments. For many years it has had no significant natural inflow but has been used largely as a storage tank, being filled by gravity from other, larger reservoirs in the hills behind it. Like all the other reservoirs in the Adelaide reticulation system, the one at Thorndon Park is carefully examined weekly, so that it is unlikely that an occurrence such as this should have been previously overlooked.

On March 7 specimens were reported as being 'numerous' in the vicinity of the control tower where the inlet valve is housed; but only two specimens were taken for identification. On March 9 a visit by Mr. Johnston disclosed none near the control tower; but eight were found in the surface waters towards the centre of the lake. On March 15 no specimens were seen; but on the following day a

dozen or so specimens were caught and as many more seen. None of these was near the control tower or the banks. On March 29 there were still many medusæ present, and those caught were appreciably larger than those taken previously. Their gonads showed a few well-developed ova, but had the appearance of being partly or almost wholly spent. Several of these had as many as three or four semi-digested daphnids in the gastro-vascular cavity. During March, the water temperature has varied between 21° and 22° C. Despite an intensive search, no specimens of the hydroid stage have been found.

Specimens varied in size from a little less than 1 cm. across the disk to nearly 2 cm. All were females. A few have been kept alive in laboratory aquaria for more than three weeks, during which time some grew appreciably and were observed to have fed on daphnids, cyprids and small mosquito larvæ.

It has been ascertained that no new water plants or animals have been intentionally introduced into the reservoir for many years. The only record is of English perch having been introduced soon after the reservoir was established. The possibility of frustules formed by gemmation from the hydroid having been carried in with water from other reservoirs and becoming established at Thorndon Park cannot be overlooked; but no medusæ have as yet been seen elsewhere. How *Craspedacusta* came to this reservoir remains as puzzling as has been its sudden appearances in many other natural and artificial waters in other parts of the world.

I. M. Thomas

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April 12.

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Birefringence of Amœbæ

It has been known for some time that the cell membrane of an amœba in water is birefringent. The optical axis lies radially, and the sign is positive with respect to the tangent[1] (Fig. 1). I have found that if an *Amœba proteus* is fixed for about 10 min. in 4 per cent formalin and then immersed in a solution of potassium mercuric iodide of refractive index 1·56, the birefringence of the membrane decreases, and the sign becomes negative (Fig. 2). A similar increase in the negative birefringence of the cell membrane on imbibition with liquids of high refractive index has also been found with red blood cell ghosts[2,3], and with sea urchin eggs[4]. It implies that the membrane has positive form birefringence and negative intrinsic birefringence. I have discussed the implications of this phenomenon, with special reference to the red cell ghost, in another communication[5].

No birefringence can be detected in the axial regions of a pseudopodium, living or imbibed, even with a very sensitive polarizing microscope. This is in contrast to the elongated processes of snail amœbocytes, or tissue culture cells, which show birefringence, the sign being positive with respect to the length of the process (Fig. 3). This birefringence may, however, be due to the stretched cell membrane rather than to the cytoplasm.

There are no striking differences in the birefringence of different regions of the membrane of a moving amœba. Small differences of retardation occur and may be due to changes either of the curvature or thickness of the membrane, or of its coefficient of birefringence. It is impossible to detect any flow birefringence in the fluid cytoplasm.

Teitel Bernard[6] found that the birefringence of leucocyte nuclei was increased by staining. This also occurs with the surface layers of amœbæ. If a living amœba is placed in dilute solutions of certain basic dyes, the birefringence at the periphery is considerably enhanced and the colour becomes a characteristic greenish-yellow. Of the dyes tested, the following were found to cause this enhancement of birefringence: Toluidine Blue, Methylene Blue, Thionin, Methyl Violet, Janus Green B, Neutral Red and Basic Fuchsin. In dilute solutions (down to 1 : 100,000 for Toluidine Blue), amœbæ which showed this enhanced birefringence continued to move about, though their activity was less than under normal conditions.

Although the effect of these dyes on the birefringence is detectable without a compensator, the most striking effect is obtained if a compensator is used. The colour of the birefringent parts of the amœba then changes, and becomes red or orange in one pair of quadrants, and green or yellow in the other pair. The colours in the quadrants are reversed if the sign of the retardation produced by the compensator is reversed. These are not the usual birefringence colours produced in white light, but are due to the dye molecules or aggregates being positively birefringent for one end of the spectrum, and negatively birefringent for the other end[6]. It should be noted

Fig. 1. Living amœba in polarized light. With compensation. × 200

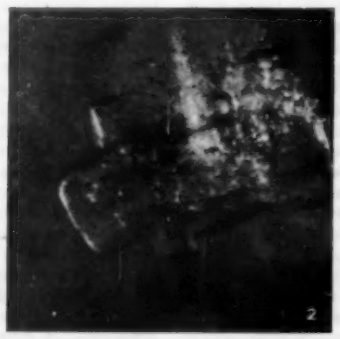

Fig. 2. Formalin-fixed amœba in potassium mercuric iodide solution in polarized light. Same compensation as in Fig. 1. × 400

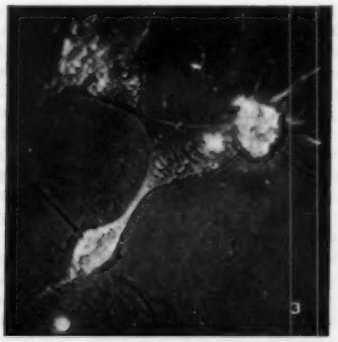

Fig. 3. Living snail amœbocytes in polarized light. With compensation. × 560

that in a few cases these colours are not the same for equivalent quadrants in different parts of one animal. The dyed membrane may then be both red and green in the same quadrant.

The presence of these colours shows that the dye molecules or aggregates are oriented in the living amœba. It seems likely that they are adsorbed on to a labile oriented structure present in the living membrane or cortex. This idea is supported by the fact that the colours vanish at once if the amœba is killed by fixatives, detergents, heat or cyanide. The addition of a weak solution of the detergent 'Teepol' to a dyed amœba in water causes the colours to vanish instantly; but only after a minute or so is there any cytolysis visible under an ordinary microscope. The dye penetrates both living and dead amœbæ, since under an ordinary microscope these appear stained with the normal colour of the dye. Only in the living animal, however, is the dye oriented.

It does not seem possible to reach any detailed conclusions about the orientation of the dyes, or about the structure on which they are presumably adsorbed. The birefringence of dyes has not yet been fully investigated, nor is it known on to what structures, or in what way, are they likely to be adsorbed.

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April 26.

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Preparation of Standardized Actinomycete Colonies

Many soil actinomycetes of the genus *Streptomyces* inhibit the growth of fungi on solid agar media, the inhibitory power exerted by a colony of such an actinomycete on a neighbouring fungal colony being indicated by the width of the inhibition zone which forms between them. Since the width of this zone is affected by the size and relative positions of the two colonies, it is essential to standardize these conditions in order to compare the anti-fungal activity of an actinomycete on different media. Actinomycetes grow slowly by comparison with most fungi; hence, when making an antagonism test of this type, it is convenient to inoculate the actinomycete over an area of the agar surface upon which will arise a colony large enough to give an easily measurable inhibition zone in a short time. Colonies 5–10 mm. in diameter when three to five days old have been found to be quite suitable. The technique of placing aliquot drops of liquid inoculum directly on an agar surface is sometimes not satisfactory, because the drops may spread, particularly when the plate is moved, thereby giving rise to irregular colonies. Moreover, the amount of spreading is affected by the composition of the medium. Again, it is sometimes necessary to inoculate with the actinomycete after the fungus has grown for some time on the plate. In such cases it is difficult to place the drops at a predetermined distance from the fungal growth.

Standardized actinomycete colonies can be obtained easily with the aid of short open-ended porcelain cylinders similar to those originally recommended for the biological assay of penicillin solutions[1]. Cylinders are dry-sterilized in Petri dishes which are then kept at a constant temperature on a hot plate while the cylinders are being removed for use[2]. A temperature of 100–110° C. is optimal for this purpose. A cylinder at this temperature, when placed end-on to an agar surface, will sink in to a depth of about 0·2 mm. to form a cup which, when quite cool, receives one or two drops of inoculum from a Pasteur pipette.

During the first forty-eight hours of incubation, the inoculum-suspending liquid is absorbed into the medium, leaving the spores or mycelial fragments drawn down into the agar within the confines of the cylinder. When all traces of surface moisture near the base of the cup have disappeared (48–72 hr. incubation) the plates may be inverted for microscopic examination, and for making zone measurements. Since some cylinders will fall off when the plates are inverted, it is advisable to remove them all at this time. A sharp tap on the underside of an inverted plate is sufficient to dislodge a cylinder and allow it to fall into the lid from which it may be removed. Neat circular colonies are left in the required positions on the agar surface. Removal of cylinders from the medium with forceps is not recommended, as this procedure frequently leads to a deposition of spores round about the colony. Provided the inoculum used is sufficiently strong to give a confluent growth on the base of the cup, the sizes of such colonies, their rates of growth and their antibiotic properties vary very little on any one medium. Little advantage is gained by using cylinders to place fungal colonies, since a drop of inoculum too small to spread gives rise to a large and uniform colony. A wire loop 1 mm. in diameter is used for placing a loop of fungal inoculum at the required distance from the actinomycete growth.

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Application of the Kozeny Equation to Consolidated Porous Media

Wyllie and Rose[1] have recently directed attention to the fact that the numerical constant (k) in the Kozeny equation may exceed the value of 5, if one applies a tortuosity correction based on the electrical resistance of the system.

During the last few years, work has been carried out in these laboratories on the electrokinetic properties of the interface between the wool fibre and water, as part of which it has been necessary to determine the radius of the fibre *in situ* by permeability measurements. It has been found that, at porosities of the order of 0·8, k may have values of the order of 6·5, and may be even greater at lower porosities.

It has been noticed in the course of the experimental work that, contrary to expectation, the volume flow-rate was not proportional to the applied pressure. A consideration of the criteria for streamline flow showed that the linear flow relation will only be found experimentally under the double condition

that there is streamline flow in the liquid and that the solid surface is geometrically smooth. This second condition is not obeyed in the case of the wool fibre, and it is likely to be equally invalid for the flow of fluids through particulate beds. The immediate consequence is that a non-linear flow function will be observed; and it can be shown qualitatively that a relation of the Kozeny type will only hold at low pressures where the flow is hydrodynamically similar to that over a smooth surface.

An application of these principles to the study of the flow of carbon tetrachloride and petroleum ether through long wool fibres packed randomly in a spherical cell and oriented parallel to the axis of a cylindrical cell showed that, in the porosity range 0·82–0·86, the data were independent of the type of packing and followed fairly closely the function

$$\log_{10} k = \text{const.} - b \log_{10} [1/(1 - \varepsilon)],$$

where ε is the porosity of the bed.

It was found that, within the limits of experimental error, the value of the constant was the same for both liquids ($k_0 = 14{\cdot}9$) and that b was inversely proportional to the kinematic viscosity of the liquid. The experimentally determined values of k were of the order of 6·5 and 4·5 for carbon tetrachloride and petroleum ether respectively. The form of the equation for k suggests that its value may be greater at lower values of the porosity.

In support of these arguments, it may be stated that the above relation has been used to calculate the k function for water, which cannot be determined experimentally because of the unknown effect of swelling on the fibre radius[3]. This function has been applied to the calculation of the fibre radius in the presence of a dilute solution of potassium chloride. In the only set of data so far examined, the radius was found to be $12{\cdot}2\,\mu$ with a standard error of $\pm 0{\cdot}14\,\mu$, based on the mean of three replicate determinations on the same cell packing. Within the limits of experimental error, this agrees with an estimate based on the direct determination of the radius after free swelling in the salt solution.

In the course of this work, it has been necessary to consider the electrical conductivity of the fibre pads, and, although comment cannot be made on the work of Wyllie and Rose until it is published in full, the following observations may be of interest.

It is a further consequence of the arguments which have been developed that, at moderate pressures, the flow-rate per unit pressure may reach a second lower and constant value due to a hydrodynamic condition approximating to the rectilinear flow of fluid through the bed. The ratio of the two constant flow-rates may be used as an estimate of the fluid dead-space in the bed under rectilinear flow conditions. Now the flow of electric current is essentially rectilinear in the case of a conducting solid and, with one further reasonable assumption, it is possible to write down an expression for the conductivity of the diaphragm in terms of the specific conductivities of the solid and the liquid. From the data mentioned earlier, the ratio of the two specific conductivities was found to be 0·2. This compares favourably with a value of 0·16 for the salt partition coefficient between the fibre and the solution, based on measured changes in the chloride ion concentration of the liquid phase.

A fuller account of the permeability investigation will be submitted elsewhere in the near future; but a detailed consideration of the conductivity problem must await the completion of the calculations now in progress.

I wish to thank the Director of the British Launderers' Research Association for permission to publish this note.

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June 22.

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A Modification to Gabor's Proposed Diffraction Microscope

Dr. D. Gabor[1] has described a new method whereby an image of an object is reconstructed from a diffraction pattern formed by the interference of the coherently scattered waves from the object and a background wave from a highly coherent source. In the system he suggested, the source is a highly demagnified image of an electron source. The object, small compared with the beam cross-section, is placed closely in front of the aberration caustic, and the scattered wave interferes with the main wave at a photographic plate placed some distance after the object. Reconstruction is carried out in an optical (light) system, which produces an irradiating wave simulating the aberrations in the electron optical system.

Experimental proof of the theoretical predictions was obtained by Gabor and later by ourselves by reconstructing diffraction patterns produced in a light optical system with light.

Experiments have been in progress in this laboratory in close association with Dr. Gabor, with the view of making electron diffraction patterns and reconstructing them with light. The apparatus used follows Gabor's suggestion, and has been realized by mounting the object in an additional mechanical stage after the projector lens of a more or less standard electron microscope. The lens system performs the function of producing the highly coherent irradiating beam.

So far, only limited success has been obtained. This has been at least partly due to the fact that the projected image is greatly distorted. Furthermore, the useful field is severely limited by chromatic difference in magnification. These factors render the alignment of the instrument and object very difficult.

It is now suggested that this modified arrangement of the electron microscope is not necessary, and, in fact, that it is advantageous to insert the object in the normal position before the objective lens. An approximate theory of the proposed arrangement has been developed. The diffraction pattern is substantially the same as in the old arrangement, except that no image distortion now occurs and the useful field is no longer limited by chromatic difference in magnification.

The conditions for coherence of the source are met with relative ease by the insertion of an aperture of a few microns in size after the electron gun, or by using a strongly demagnifying condenser lens.

The new arrangement allows the electron optical system to be aligned with comparative ease, and the object can be located by using the instrument as a normal transmission microscope; a photograph may

be taken in this condition. The diffraction pattern is then photographed after defocusing the condenser lens to increase the coherence. Reconstruction should then give additional resolution.

It is of interest to note that the state of focus is relatively unimportant in producing the diffraction picture. As the instrument is defocused, more of the information concerning small detail is transferred from the normal image to the diffraction fringes. At focus, all the information which the aberrations allow is contained in the normal image. This we may expect, since the aberrations prevent true focusing. The focused image may be reconstructed to give the improved resolution set by the coherence.

The ultimate resolution possible after reconstruction may be judged from the diffraction pattern by the width of the last and narrowest fringe; this is independent of the position of focus and equal to twice the resolving limit.

It is still a necessary requirement that the object take up only a small proportion of the total area occupied by the background interfering beam. This may be regarded as one aspect of the fundamental coherence requirement.

Reconstruction apparatus for the new arrangement has been considered and does not appear to present any special additional difficulties.

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April 20.

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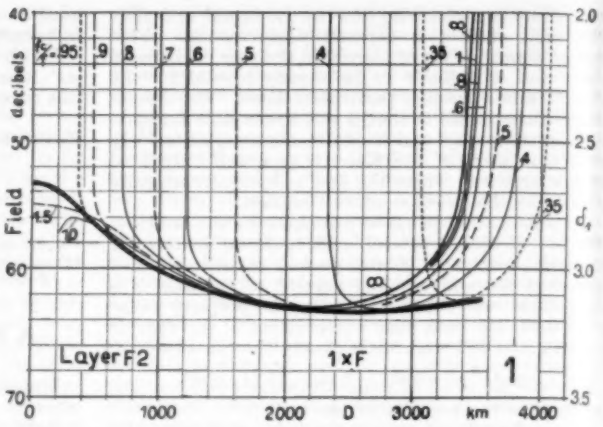
Geometrical Optics of Ionospheric Propagation

Lejay and Lepechinsky[1] recently published a note on field intensity as a function of distance, a question which is of great interest for ionospheric prediction work. With their method of the reflectrix they find two focusing effects, one at a distance corresponding to a path that leaves the earth tangentially, the other at the limit of the skip distance.

The first effect is noted as "an already known fact". In fact, consideration of this effect is one of the fundamental ideas of the ionospheric prediction method, used in Germany during the War (since 1941). I have given a detailed calculation in a report published in 1943 [2], and, since the War, the essential results have been published in France[3]. The second effect was calculated for the first time in an early work of Försterling and Lassen[4], and the same work also contains a theory of the so-called Pedersen-ray.

Meanwhile, a much more complete treatment of the problem has been undertaken[5]. In the case of a parabolic distribution of electron density (earth and ionosphere being curved), the 'geometrical optics' of the ionosphere has been studied by means of an extension of Försterling and Lassen's methods. Theoretically, there are three focusing effects: (1) for the skip distance, resulting from refraction phenomena, (2) for the maximum length of path (tangent ray), due to the curvature of the reflecting layer,



(3) for the antipodes, brought about by the spherical form of the earth. The third effect will, in practice, be reduced greatly by irregularities of the reflecting layer.

The first effect, which can be very important in certain cases, corresponds to a distance that can never be fixed. For practical use, neither the first nor the third effect can be applied regularly. The second effect is also influenced by variations of electron density (and layer height). We began by making exact calculations for a given parabolic model of ionospheric layers (limits 240/432 for the F-layer, 100/150 for the E-layer). The various curves of field intensity correspond to all possible ratios of critical to working frequency (f_c versus f) (see graph). We now draw a curve through the lower limits of these curves[6]; this thick curve is used for our prediction work. Thus we find curves for the different paths $1 \times F$, $2 \times F$, $3 \times F$ . . . $1 \times E$, $2 \times E$ . . . For distances of about 20,000 km. the influence of the third focusing effect has been eliminated. The resulting curves are not greatly different from those formerly used[2,3], the influence of curvature being the most important one. Field intensities observed at great distances cannot well be explained, if one does not take this second effect into account.

The work mentioned above[5,6] forms part of the research work of the Service de Prévision Ionosphérique Militaire (France).

K. Rawer

Service de Prévision Ionosphérique Militaire,
Freiburg, Germany.
May 25.

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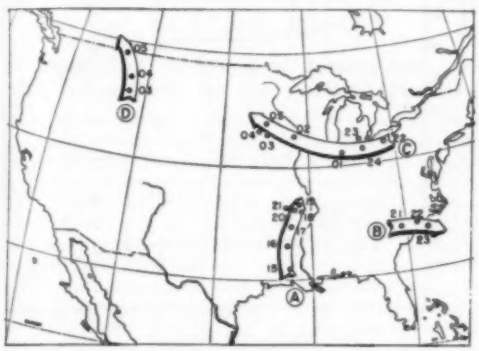
Large-scale Sporadic Movements of the *E*-Layer of the Ionosphere

A widespread effort is at present being made to obtain information on the prevalence and occurrence of sporadic E-layer reflexions over the North American continent. Such information is supplied by a network of volunteer radio amateurs (operating in the vicinity of 50 mc./s.), upon whose co-operation the success of the project depends.

Some very preliminary results are available, and it is the intention of this short note to indicate striking movements during the period May 15–16, 1949, G.M.T., the latest data available at the time of writing. Results are shown in the accompanying sketch-map summarizing *E*-layer reflexions at times centred on the hours 1500 G.M.T., May 15, 1949, to 0500 G.M.T., May 16, 1949, inclusive. In this diagram a circle represents the 'centre of mass' of the distinct reflexion region shown, and the numeral represents the hour, G.M.T. The observed internal consistency between single- and double-hop reflexion areas was very gratifying and strengthened belief in the accuracy of the data. It seems premature to attempt determination of equivalent ionic concentrations, inasmuch as present theories on sporadic *E*-regions attribute reflexion to either a region of high electron density or a volume of patchy ionic concentration.



Summary plot indicating movement of four sporadic *E*-region reflexion areas during May 15–16, 1949. Numbers represent hours G.M.T.

Several limitations on the employment of the data should be noted. Some bias is inherent in the results because of unknown observational factors of time and space. Thus, it is not definitely known what percentage of, or definitely which, amateurs were 'on the air' prior to 1500 G.M.T.; further, with respect to their spatial distribution, the concentration of observers east of the Rocky Mountains is fairly good, but that west of the mountains is somewhat sparse. Also, sporadic *E*-regions around the extreme (north or south) coastal areas of the continent cannot be observed because of the dearth of shipboard operators co-operating in this venture. Although it is hoped that they will increase, the present number of volunteer observers in the Dominion of Canada and in Mexico is also somewhat small. Furthermore, the density of observed sporadic *E*-layer reflexion points is influenced by the varying number of amateurs actively receiving or transmitting.

It should also be realized that a gradual change in altitude of the reflexion or scattering area, when observed at a single radio-frequency, may indicate the appearance or disappearance of a sporadic *E*-layer. However, in spite of these limitations, fairly good, consistent results have been obtained during the time interval shown.

In examining the results, several interesting effects may be noted. At 1500 G.M.T. a few scattered reflexion points were observed in reflecting region *A* near the Gulf of Mexico. The number of these points increased rapidly during the following hour to form a well-defined area which moved rapidly to the north for the next two hours at an average speed of about 185 km./hr. During 1800–2100 G.M.T. this reflecting area seemed to remain almost stationary and to dissipate in intensity. Dissipation also accompanied a slowing down of reflexion region *C*. While region *A* disintegrated, cloud *B* appeared to form, and, during the next three hours, moved to the east at a speed of about 210 km./hr. Reflecting area *B* was apparently lost as it crossed the coastline.

Region *C* was observed for the greatest length of time. Appearing as a few points at 2200 G.M.T., the number of reflexions increased rapidly until 0300 G.M.T. Simultaneously, a somewhat rapid movement to the west is indicated. The average velocity during 2200–0100 G.M.T. is about 125 km./hr. (from the east). The average velocity of about 370 km./hr. observed, during the next hour, is regarded as doubtful since it is difficult to conceive of an accelerating mechanism of such magnitude during the short time-interval available. The following hour the movement has slowed down to about 210 km./hr., and during succeeding hours dissipation occurs with very little movement. Reflecting region *D* indicates a movement to the north at about 180 km./hr. during 0300–0500 G.M.T.

Whether these results indicate that there is actual atmospheric motion or only electron drift is not certainly known. The possibility of some type of anticyclonic motion in the upper atmosphere is suggested by the combined motion of areas *A* and *B*, and *C* and *D*; but it is far too early to state on the basis of present evidence that such circulations exist.

On some occasions, two amateurs not normally in contact because of distance were suddenly able to communicate for a period up to several minutes or even longer. These contacts were characterized by a sudden beginning of contact and usually by a sudden ending. As meteoric ionization has been known to persist from seconds to minutes and sometimes for as long as several hours, electron clouds caused by meteors may account for isolated instances of long-range contact being reported as due to sporadic *E*-regions.

This study could not have been accomplished without the wholehearted and active co-operation of a great many radio amateurs operating in North America. Appreciation is also expressed to Mr. O. P. Ferrell for screening, and Messrs. R. J. Donaldson, jun., and S. Enderson for plotting, the data.

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Arc Spectrum of Gallium: New Absorption Lines in the Schumann Region

THE list of known terms of GaI as compiled by Bacher and Goudsmit[1], while not very extensive, constitutes the best data so far available. Of this, the series terms are based on Fowler[2], Paschen-Götze[3], and measurements of Uhler and Tanch[4]; the only other terms quoted, namely, $4s4p^2\ ^2S$ and ^4P, are from Sawyer and Lang[5].

The following points arise with regard to these data:

(1) There are only two known ^2P terms, apart from the ground term. The longest wave-length doublet of the principal series has a calculated position λλ 11,940, 12,096 A., and, judging from Megger's work on infra-red spectra, it should be

possible to record these lines on modern infra-red plates. In addition, there would appear to be no obvious difficulty in the way of extending the series to higher members.

(2) There is an error in Bacher and Goudsmit's tabulation of $8s\ ^2S_{1/2}$, which by examination of Uhler and Tanch's measurements is seen to lie at 4,048 cm.$^{-1}$.

(3) While the $sp^3\ ^4P$ term of Sawyer and Lang is scarcely in doubt, the position they suggested for ^2S of the same configuration is in marked disagreement with that to be expected from identifications in iso-electronic spectra.

Following on the experiments, already reported[6], on the far ultra-violet absorption spectrum of indium vapour, exploratory experiments of similar type have been made with gallium, at temperatures up to 1,620° C. Six intense absorption lines readily appeared on the background provided by the many-line spectrum of H_2, in the wave-length range 1500–1650 A. Four of these are identified as the PP' multiplet $4\ ^2P^0_{1/2\ 3/2} - 4s4p^2\ ^2P_{1/2\ 3/2}$, and the other two, which exhibit the marked diffuseness indicative of auto-ionization, constitute the doublet $4\ ^2P^0_{1/2\ 3/2} - 4s4p^2\ ^2S_{1/2}$.

Approximate positions of the resulting new levels, based on rather rough initial measurements, are:

$$4s4p^2\ ^2P_{3/2} - 18{,}042 \text{ cm.}^{-1}.$$
$$^2P_{1/2} - 17{,}416$$
$$^2S_{1/2} - 13{,}720$$

A full account of this work, and of experiments in progress, will appear later.

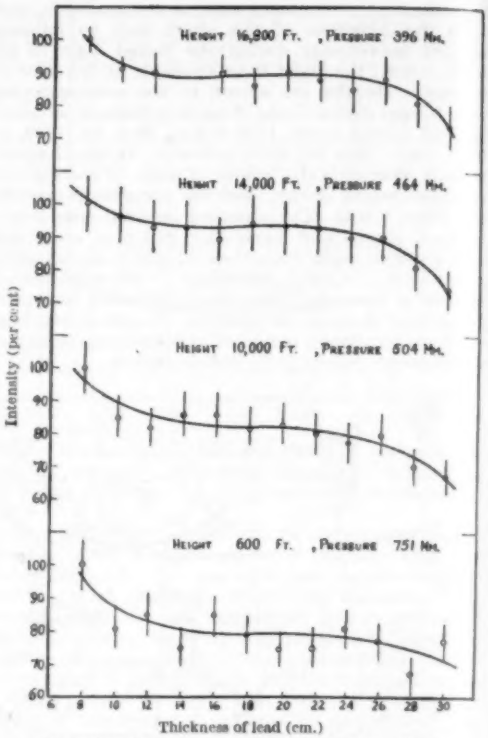
W. R. S. Garton
Imperial College of Science and Technology,
London, S.W.7.
April 19.

[1] "Atomic Energy States" (McGraw-Hill, New York, 1932).
[2] "Report on Series in Line Spectra" (London, 1922).
[3] "Seriengesetze der Linienspektren" (Springer, Berlin, 1922).
[4] Uhler, H. S., and Tanch, J. W., *Astrophys. J.*, **55**, 291 (1922).
[5] Sawyer, R. A., and Lang, R. J., *Phys. Rev.*, **34**, 712 (1929).
[6] Garton, W. R. S., *Nature* [**166**, 150 (1950)].

Lead Absorption of Cosmic Rays at Different Altitudes near Magnetic Latitude 22° N.

Anomalies of the absorption curve of vertically incident cosmic rays in lead have been reported[1–6]. Clay and his associates[1–3] showed the existence of a second and third maximum in the ionization curve at about 16 and 25 cm. of lead. Chandrashekhar Aiya[4] at Bangalore reported a drop in his intensity curve at 21 cm. of lead. Swann and Morris[5] at Bocayuva found a drop at a lead thickness of 22 cm., whereas there was no apparent drop at Swarthmore. Recently, Fenyves and Haiman[7] at Budapest observed anomalies in their absorption curve in lead at 18·2 cm. and 26·6 cm.

In 1945, I made some measurements on the absorption of cosmic rays in lead near magnetic latitude 22° N. at altitudes varying from 600 ft. to 16,800 ft. in the Himalayas. Two similar telescopes consisting of three Geiger–Müller tubes each with slabs of lead interposed, connected together in a coincidence circuit, were used, and thickness of lead above the telescopes was varied from zero to 20 cm. in steps of 4 cm. The solid cones subtended by the two telescopes were the same. The coincidence set


Height 16,800 Ft. , Pressure 396 Mm.
Height 14,000 Ft. , Pressure 464 Mm.
Height 10,000 Ft. , Pressure 604 Mm.
Height 600 Ft. , Pressure 751 Mm.
Intensity (per cent)
Thickness of lead (cm.)

Absorption of cosmic rays in lead at different elevations

connected to the upper telescope measured the coincidences for 8, 12, 16, 20, 24 and 28 cm. of lead thicknesses, while the lower one recorded the coincidences for 10, 14, 18, 22, 26 and 30 cm. of lead. The altitudes tried were 600 ft., 10,000 ft., 14,000 ft. and 16,800 ft. above sea-level.

The results are shown in the accompanying graph, where intensity (per cent) is plotted against absorber thickness. The general form of the curves is similar to that of other workers. It may be observed that up to a thickness of 12 cm. of lead each curve shows a rapid decrease, and from there on there is no appreciable decrease in intensity until the thickness of lead exceeds 25 cm. Abnormalities are shown in all the four curves. Beyond 25 cm. of lead, intensity shows a definite drop. This drop occurs at the same thickness of lead at all altitudes.

George and Appapillai[8] measured the absorption of cosmic rays at Colombo and London at sea-level. Their curves are similar to those reproduced here, except that the downward bend in their curves occurs at 18 and 15 cm. at London and Colombo respectively. Fenyves and Haiman's[7] data show maxima at 18·2 cm. and 26·6 cm., whereas the curve nearer to sea-level in the present paper indicates these maxima with a shift of about two centimetres to smaller thickness, namely, near 16 cm. and 24 cm. Since these measurements were made for a different purpose, our statistical accuracy cannot bring out the details; but one point is clear, and that is that there exists the abnormality in the intensity curves in the form of a drop beyond 25 cm. of lead.

There is no doubt that beyond 20 cm. the sudden drop in the intensity versus lead-thickness curve in

lower latitudes is a real one, and the question of its presence at higher latitudes is debatable. The fact that the drop in the intensity curve at all elevations occurs at the same thickness of lead near magnetic latitude 22° N. supports the suggestion of Swann and Morris[5] that it is concerned with something happening in the lead and does not depend on the energy of the rays. It is intended to investigate this point in more detail in these latitudes.

P. S. Gill

Muslim University,
Aligarh.
April 4.

[1] Clay, J., *Physica*, **3**, 332 (1936).
[2] Clay, J., Gemert and Wiersma, *Physica*, **3**, 627 (1937).
[3] Clay, J., Venema and Jonker, *Physica*, **7**, 673 (1940).
[4] Aiya, Chandrashekhar S. V., *Nature*, **153**, 375 (1944).
[5] Swann, W. F. G., and Morris, P. A., *Phys. Rev.*, **72**, 1262 (1947).
[6] George, E. P., and Appapillai, V., *Nature*, **155**, 726 (1945).
[7] Fenyves, E., and Haiman, O., *Nature*, **165**, 244 (1950).

Statistical Analysis of Results for Successive Tests on the same Organism

In a recent letter[1], Leech has pointed out an error of method which sometimes occurs in the analysis of experimental data; this error "arises from regarding successive tests on the same animal as independent". With this criticism I am in complete agreement. However, as an example of this error, he refers, *inter alia*, to a paper[2] for the statistical analysis in which I am responsible. Bailey also, in a review[3] of this paper, has made a similar criticism. The purpose of this note is to explain the method of analysis used, to indicate how it may be employed where the independence of successive observations cannot be assumed, and to point out that the criticisms of Bailey and Leech do not apply in this particular case.

In the experiment under consideration, the animals were divided into two groups, one treated and one untreated. The treatment was continued over four experimental periods, during each of which measurements of various physical characters were taken for each animal. In determining the treatment effect, the relevant comparison is not the main treatment comparison, but the interaction of treatments and periods. The interaction measures the progressive change, due to the treatment, of the difference between the two groups. On the hypothesis of no-treatment effect, the mean squares for the treatment-period interaction and the cow-period interaction can be shown to have the same expectation, whether or not successive observations on the same animal are independent. Consequently, a comparison of the two mean squares provides a valid test of significance for the relevant treatment effects.

In the published paper[2], only the bare essentials of the statistical analysis have been presented, and this may have led to some misunderstanding. The mean squares compared in Table 1 are those for treatment-period interaction and cow-period interaction, which, as already explained, give a valid test of significance.

Finally, with reference to a criticism of Bailey[3], the standard errors quoted for measurements taken at the beginning and end of the experiment were not intended for use in testing significance, but only to indicate the variability of the results. All the significance judgments are based on the analyses of variance. When measurements are taken at autopsy only, the standard errors are then, of course, appropriate for testing the significance of the corresponding differences.

E. J. Williams

Section of Mathematical Statistics,
c/o Division of Forest Products,
Commonwealth Scientific and
Industrial Research Organisation,
South Melbourne.
April 26.

[1] Leech, F. B., *Nature*, **165**, 323 (1950).
[2] McQuillan, M. T., Trikojus, V. M., Campbell, A. D., and Turner, A. W., *Brit. J. Exp. Path.*, **29**, 93 (1948).
[3] Bailey, G. L., *Vet. Bull.*, **19**, 421 (1949).

In the paper referred to, Mr. Williams has avoided the error of method originally attacked, and his analysis has undoubtedly led to correct inferences being made. A theoretical criticism which may be of consequence when the experimental results are less definite can be illustrated by a simplified example.

Suppose that twelve animals are allocated at random to two equal groups receiving different treatments, and that measurements are made on each animal in three successive periods. It is convenient to replace the series of measurements on each animal by its mean and linear and quadratic components. This leads to the following analysis of variance:

			Degrees of freedom
Item 1	Periods		2
2	Treatments		1
3	Treatments × periods	—linear	1
4		—quadratic	1
5	Animals		10
6	Animals × periods	—linear	10
7		—quadratic	10
		Total	35

The average effects of treatment on the mean measurements and on the linear and quadratic components can be estimated, and tests of significance which are separately valid can be made by comparing items 2, 3 and 4 with items 5, 6 and 7 respectively, the latter three items also providing estimates of the standard errors appropriate to these effects. If items 3 and 4 are pooled and compared with a pooled error taken from items 6 and 7, the resulting variance ratio will have an expected value of 1 on the null hypothesis; but in the situation which often occurs in animal experimentation, when item 6 is substantially larger than item 7, the ratio will not follow the F-distribution with 2 and 20 degrees of freedom. This procedure may also conceal a significant linear effect by pooling it with a negligible quadratic term.

The problem of obtaining the most efficient estimate of treatment differences when, for example, these differences increase steadily as the experiment progresses, is more complicated; in essence, the required estimate in this case will be a linear function of the mean and linear components, with coefficients depending on the variances and covariance of these components. Once the coefficients have been determined, the linear function can be calculated for each animal separately, and standard errors and tests of significance can be obtained by carrying out an ordinary analysis of variance on these values.

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Harpenden, Herts.

F. B. Leech

Veterinary Laboratory,
Ministry of Agriculture and Fisheries,
New Haw, Weybridge,
Surrey.

FORTHCOMING EVENT

Monday, August 21—Saturday, August 26

INTERNATIONAL SOCIETY OF HAEMATOLOGY (at Cambridge).—Congress.

APPOINTMENTS VACANT

APPLICATIONS are invited for the following appointments on or before the dates mentioned:

LECTURER (with qualifications and experience in structural engineering and, preferably, a university degree) IN THE DEPARTMENT OF ENGINEERING, County Technical College, Wednesbury—The Director of Education, Department F.E., County Education Offices, Stafford (August 26).

SUPERINTENDENT and an ASSISTANT SUPERINTENDENT IN THE CHEMISTRY DIVISION in London—The Secretary, Railway Executive, 222 Marylebone Road, London, N.W.1 (August 26).

ASSISTANT IN THE BIOCHEMISTRY DEPARTMENT, and an ASSISTANT IN THE CHEMISTRY DEPARTMENT—The Secretary, The University, Aberdeen (August 31).

ASSISTANT PHYSICIST for duties in the Radiotherapy and X-Ray Diagnostic Departments—The Clerk of the Governors, St. Thomas's Hospital, London, S.E.1 (August 31).

CHEMIST of B.Sc. (Special) standard to take part in an investigation of urinary steroids in clinical cases—The Dean, Guy's Hospital Medical School, London Bridge, London, S.E.1 (August 31).

DIRECTOR OF THE NEW HORTICULTURAL CENTRE of the Ministry of Agriculture at Loughall, County Armagh—The Secretary, Civil Service Commission, Stormont, Belfast (August 31).

LECTURER IN FOOD SCIENCE—The Secretary, Royal Technical College, Glasgow (August 31).

LECTURER IN MATHEMATICAL PHYSICS—The Secretary, The University, Edinburgh (August 31).

LECTURER IN MATHEMATICS at the University of Hong Kong—The Secretary, Association of Universities of the British Commonwealth, 5 Gordon Square, London, W.C.1 (August 31).

LECTURER IN METALLURGY—The Registrar, University College, Southampton (August 31).

LECTURER IN PHYSICS AND MATHEMATICS at the Technical College of Monmouthshire—The Director of Education, County Hall, Newport, Mon. (August 31).

LECTURER (with a Social Science diploma or certificate, and practical experience in social work) IN THE SCHOOL OF SOCIAL SCIENCE, Victoria University College, Wellington, New Zealand—The Secretary, Association of Universities of the British Commonwealth, 5 Gordon Square, London, W.C.1 (August 31).

ASSISTANT LECTURER IN PHYSIOLOGY, an ASSISTANT LECTURER IN BIOCHEMISTRY, and an ASSISTANT LECTURER IN BIOPHYSICS—The Registrar, University College, Cathays Park, Cardiff (September 1).

ASSISTANT LECTURER IN PURE MATHEMATICS—The Registrar, University College, Hull (September 2).

DEMONSTRATOR IN PHYSIOLOGY—The Registrar, The University, Leeds 2 (September 4).

PRINCIPAL RESEARCH OFFICER or SENIOR RESEARCH OFFICER IN THE DIVISION OF INDUSTRIAL CHEMISTRY (Cement and Ceramics Section) of the C.S.I.R.O., at Fishermen's Bend, Melbourne, to conduct fundamental investigation on the structure and properties of clays and similar minerals—The Chief Scientific Liaison Officer, Australian Scientific Liaison Office, Africa House, Kingsway, London, W.C.2, quoting No. 2965 (September 9).

SENIOR ASSISTANT BACTERIOLOGIST in the Water Examination Department—The Clerk of the Metropolitan Water Board, New River Head, Rosebery Avenue, London, E.C.1, endorsed 'Senior Assistant Bacteriologist' (September 9).

W. T. HENLEY FELLOWSHIP for research in electrical engineering—The Registrar, Queen Mary College, Mile End Road, London, E.1 (September 15).

DEPUTY PRINCIPAL, a LECTURER IN FORESTRY MANAGEMENT, and a LECTURER IN BIOLOGY, in the Australian Forestry School, Canberra—The Australian High Commissioner, Australia House, Strand, London, W.C.2 (Canberra, September 16).

LECTURER or SENIOR LECTURER IN GEOLOGY (with special qualifications in economic or engineering geology with petrology) at the University of Sydney—The Secretary, Association of Universities of the British Commonwealth, 5 Gordon Square, London, W.C.1 (Sydney, September 21).

LECTURER IN MECHANICAL ENGINEERING at the University of Melbourne—The Secretary, Association of Universities of the British Commonwealth, 5 Gordon Square, London, W.C.1 (September 30).

PROFESSOR OF ELECTRICAL ENGINEERING in the University of Manchester and in the College of Technology—The Registrar, College of Technology, Manchester 1 (September 30).

PROFESSOR OF TECHNOLOGICAL CHEMISTRY in the University of Manchester and in the College of Technology—The Registrar, College of Technology, Manchester 1 (October 23).

ASSISTANT LECTURER AND DEMONSTRATOR IN THE CHEMISTRY DEPARTMENT—The Secretary, King's College of Household and Social Science, Campden Hill Road, London, W.8.

ASSISTANT LECTURER for teaching pharmaceutical subjects—The Secretary, Royal Technical College, Glasgow.

CHEMISTS or JUNIOR CHEMISTS (with a science degree and, preferably, some research experience in either organic or physical chemistry)—The Director of Research, British Rubber Producers' Research Association, 48 Tewin Road, Welwyn Garden City, Herts.

LECTURER IN REFRIGERATION at the National College for Heating, Ventilating, Refrigeration and Fan Engineering—The Clerk to the Governors, Borough Polytechnic, Borough Road, London, S.E.1.

REPORTS and other PUBLICATIONS

(not included in the monthly Books Supplement)

Great Britain and Ireland

The Education of the Young Worker: Report of the Second Conference held at Oxford in July 1949 under the auspices of the University Department of Education. (Published for King George's Jubilee Trust.) Pp. 84. (London: Oxford University Press, 1950.) 2s. 6d. net. [266

British Trust for Ornithology. Sixteenth Annual Report, 1949. Pp. 48. (Oxford: British Trust for Ornithology, 1950.) [270

Memorandum on Faults in Arc Welds in Mild and Low Alloy Steels. Pp. 39. (London: British Welding Research Association, 1950.) 2s. 6d. [276

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Medical Research Council. Memorandum No. 24: The Causes of Blindness in England and Wales. By Arnold Sorsby. Pp. vi+42. (London: H.M. Stationery Office, 1950.) 1s. 6d. net. [286

Science Museum. Handbook of the Collections illustrating Time Measurement. Part 2: Descriptive Catalogue. By Dr. F. A. B. Ward. Second edition. Pp. 95+10 plates. (London: H.M. Stationery Office, 1950.) 3s. net. [296

Department of Scientific and Industrial Research. Methods for the Detection of Toxic Gases in Industry, Leaflet No. 7: Carbon Monoxide. Revised edition. Pp. ii+6. (London: H.M. Stationery Office, 1950.) 6d. net. [296

Operational Research: its Application to Peace-time Industry. Pp. 152. (Manchester: Manchester Joint Research Council, 1950.) 10s. 6d. [306

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Other Countries

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Institut pour l'Encouragement de la Recherche scientifique dans l'Industrie et l'Agriculture. Comptes Rendus de recherches, No. 3: Travaux du Centre d'Études et de Recherches sur l'Agriculture. Pp. 137. (Bruxelles: Institut pour l'Encouragement de la Recherche scientifique dans l'Industrie et l'Agriculture, 1950.) 90 francs. [306

Académie Royale de Belgique: Classe des Sciences. Mémoires, Tome 25: Notes pour l'histoire de la Botanique et de l'Horticulture en Belgique. Par E. De Wildeman. Pp. 832. (Bruxelles: Académie Royale de Belgique, 1950.) 500 francs. [37

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Commonwealth Scientific and Industrial Research Organization. Bulletin No. 241: An Australian Phytochemical Survey, 1, Alkaloids and Cyanogenetic Compounds in Queensland Plants. By L. J. Webb. Pp. 56. (Melbourne: Government Printer, 1949.) [47

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Indian Council of Agricultural Research. Miscellaneous Bulletin No. 61: The Composition of Milk. Part 1, Collection of Data, by Dr. B. H. Schneider, James N. Warner, L. D. Dharmi and B. F. Agarwal; **Part 2, Statistical Study,** by Dr. P. V. Sukhatme, V. G. Pendharkar and A. N. Sankaran. Pp. v+81. (Delhi: Manager of Publications, 1948.) 6 rupees; 9s. 6d. [57

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